PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PPD70191/WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/05250	International filing date *(day/month/year)* 03.12.2003	Priority date *(day/month/year)* 23.12.2002
International Patent Classification (IPC) or both national classification and IPC C07D471/04		
Applicant SYNGENTA PARTICIPATIONS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 88 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01.06.2004	21.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Weisbrod, T Telephone No. +49 89 2399-8931

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/05250

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-80 received on 22.10.2004 with letter of 13.10.2004

Claims, Numbers

1-14 received on 22.10.2004 with letter of 13.10.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☒ the description, pages: 81-96

   ☒ the claims, Nos.: 15-16

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item I

Basis of the opinion

1 In response to the written opinion the applicant filed an amended set of claims and a completely amended description. Amended claim 1 has been limited with the features of original dependent claims 3 and 4 ($R^2 = NR^3R^4$ and R = halo). Accordingly, original claims 3 and 4 have been deleted. In amended claim 12 (corresponding with original claim 14) the specific compound of **D2**, which falls within the scope of present formula (6), has been excluded by a proviso. Furthermore, the description has been adapted to the current set of claims and a reference to document **D1** has been inserted. The amendments appear to meet the requirements of Articles 19(2) and 34(2)(b) PCT.

2 The application is now directed to
- (i) pyridodiazines of formula (I) (claims 1-10),
- (ii) a process for preparing compounds (I) (claim 11),
- (iii) intermediates (4) to (6) and (13) (claim 12),
- (iv) a plant fungicidal composition comprising a compound (I) (claim 13), and
- (v) the corresponding method of controlling phytopathogenic fungi (claim 14).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents.

D1: US-A-5 821 244, 13.10.1998; cited in the amended application.
D2: Beilstein BRN 538395.
D3: WO 02/083676 A, 24.10.2002; cited in the application.
D4: EP-A-1 249 452, 16.10.2002; cited in the application.
D5: GB-A-1 431 063, 07.04.1976.

2 Novelty

D1 relates to condensed nitrogen heterocycles as fungicides (cf. column 14, line 56 to column 15, line 4). The present compounds (I) differ from the compounds of **D1** at

least insofar as R^1 in position 3 of the pyrido ring is different from hydrogen (cf. D1, columns 1-2, formula (I) wherein one of V and W is CR^2 and the other is CH or N). Consequently, the present claimed matter is novel vis-à-vis **D1**.

D2 shows a compound of present formula (6). This compound has been excluded from present claim 12 by means of a disclaimer. Hence, the claimed matter is novel over **D2**.

D3 and **D4** relate to triazolopyrimidines as plant fungicides. The present compounds (I) differ from those of **D3** and **D4** insofar as they represent pyrido-pyrazines and pyrido-pyridazines rather than triazolo-pyrimidines. Intermediates (3) to (6) and (13) are not disclosed in the said prior art. The present claimed matter is thus novel vis-à-vis **D3** and **D4**.

D5 discloses 3-carboxy or 3-alkoxycarbonyl pyridopyridazines as analgesic, antiinflammatory, and CNS depressant agents. The present compounds (I) differ from those of **D5** insofar as the 3-substituent R^1 is different from carboxy and alkoxycarbonyl. The present claimed matter is thus novel vis-à-vis **D5**.

The application as amended appears to comply with the criterion of novelty according to Article 33(2) PCT.

3 Inventive Step

3.1 The application describes the synthesis of certain compounds (I) and reports that such compounds are active against certain plant fungi (cf. original pages 93-96).

3.2 In view of **D1** as most relevant state of the art, the problem underlying the present application may be seen in the provision of further plant fungicides. The present compounds (I) differ from the compounds of **D1** at least insofar as R^1 is different from hydrogen. In addition, the present compounds (I) require that R is a halo group and two of the values W to Z are nitrogen. Such (R)halo-pyridodiazines are not exemplified in document **D1**. For these reasons, the present compounds (I) do not appear unequivocally obvious in view of document **D1** alone or in combination with any other cited document. Based on the substantiated antifungal activity of the present compounds (I), the present claimed matter appears thus to comply with the requirement of inventive step according to Article 33(3) PCT.

4 Further Deficiencies of the Application

The relevant background art disclosed in **D2** is not mentioned in the description, nor is this document identified therein (Rule 5.1(a)(ii) PCT).

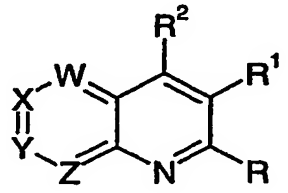
FUNGICIDES

This invention relates to novel derivatives of pyridopyrazines and pyridopyridazines, to processes for preparing them, to certain intermediate chemicals used in their manufacture, to compositions containing them and to methods of using them to combat fungi, especially fungal infections of plants.

Derivatives of the nitrogen-containing 5,6 ring system *s*-1,2,4-triazolo[1,5-a]pyrimidine are known from the patent literature as being useful for controlling phytopathogenic fungi. Examples of recent patent publications include EP-A-1249452, WO 02/051845, WO 02/083676, WO 02/083677, WO 02/088125, WO 02/088126, WO 02/088127. Condensed nitrogen heterocycles used as antimycotics are known from US 5821244. Derivatives of pyridopyrazines are known in the chemical literature, for example from *J. Med. Chem.* (1968), 11(6), 1216-18, *J. Med. Chem.* (1970), 13(5), 853-7 and US 3984412, but not for agrochemical purposes.

The present invention is concerned with the provision of novel pyridopyrazines and pyridopyridazines for combating phytopathogenic diseases on plants and harvested food crops.

Thus, according to the present invention, there is provided a compound of the general formula (1):



(1)

wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is halo, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C_{1-4})alkyl, aryl(C_{1-4})alkoxy, heteroaryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkoxy, aryl(C_{1-4})alkylthio, heteroaryl(C_{1-4})alkylthio, morpholino, piperidino or pyrrolidino;

R^2 is NR^3R^4;

R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6, provided

that not both R^3 and R^4 are H or NR^5R^6, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and

any of the foregoing aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'"R"", -NHCOR'", -NHCONR'"R"", -CONR'"R"", -SO_2R'", -OSO_2R'", -COR'", -CR'"=NR"" or -N=CR'"R"", in which R'" and R"" are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.

The invention includes a compound of the general formula (1) as defined immediately above except that: C_{1-8} alkoxy and C_{1-8} alkylthio are excluded as values of R and R^2; C_7 alkylene and C_{3-7} alkenylene are excluded as chains formed by R^3 and R^4; the C_{3-6} chain that R^3 and R^4 may form may only be optionally substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R^3 and R^4 may form; tri(C_{1-4})alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

The compounds of the invention may contain one or more asymmetric carbon atoms and may exist as enantiomers (or as pairs of diastereoisomers) or as mixtures of such. They may also exist as diastereoisomers by virtue of restricted rotation about a bond. However, mixtures of enantiomers or diastereoisomers may be separated into individual isomers or isomer pairs, and this invention embraces such isomers and mixtures thereof in all proportions. It is to be expected that for any given compound, one isomer may be more fungicidally active than another.

Except where otherwise stated, alkyl groups and alkyl moieties of alkoxy, alkylthio, etc., contain from 1 to 8, suitably from 1 to 6 and typically from 1 to 4, carbon atoms in the form of straight or branched chains. Examples are methyl, ethyl, *n*- and *iso*-propyl, *n*-, *sec*-, *iso*- and *tert*-butyl, *n*-pentyl and *n*-hexyl. Cycloalkyl groups contain from 3 to 8, typically from 3 to 6, carbon atoms and include bicycloalkyl groups such as the bicyclo[2.2.1]heptyl group. Haloalkyl groups or moieties are typically trichloromethyl or trifluoromethyl or contain a trichloromethyl or trifluoromethyl terminal group.

Except where otherwise stated, alkenyl and alkynyl moieties also contain from 2 to 8, suitably from 2 to 6 and typically from 2 to 4, carbon atoms in the form of straight or branched chains. Examples are allyl, 2-methylallyl and propargyl. Optional substituents include halo, typically fluoro. An example of halo-substituted alkenyl is 3,4,4-trifluoro-*n*-butenyl.

Halo includes fluoro, chloro, bromo and iodo. Most commonly it is fluoro, chloro or bromo and usually fluoro or chloro.

Aryl is usually phenyl but also includes naphthyl, anthryl and phenanthryl.

Heteroaryl is typically a 5- or 6-membered aromatic ring containing one or more O, N or S heteroatoms, which may be fused to one or more other aromatic or heteroaromatic rings, such as a benzene ring. Examples are thienyl, furyl, pyrrolyl, isoxazolyl, oxazolyl, oxadiazolyl, pyrazolyl, imidazolyl, triazolyl, isothiazolyl, tetrazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, benzofuryl, benzothienyl, dibenzofuryl, benzothiazolyl, benzoxazolyl, benzimidazolyl, indolyl, quinolinyl and quinoxalinyl groups and, where appropriate, N-oxides thereof.

The 6,6-ring systems embraced by the general formula (1) are pyrido[2,3-c]pyridazines (where W and X are both CR^8 and Y and Z are both N), pyrido[2,3-d]pyridazines (where W and Z are both CR^8 and X and Y are both N), pyrido[3,2-c]pyridazines (where Y

and Z are both CR^8 and W and X are both N) and pyrido[2,3-b]pyrazine (where X and Y are both CR^8 and W and Z are both N). Of particular interest are pyrido[2,3-b]pyrazines.

R^8, which may be the same or different for the two CR^8 values of W, X, Y and Z, is H, halo (for example bromo), C_{1-4} alkyl (for example methyl), C_{1-4} alkoxy (for example methoxy) or halo(C_{1-4})alkyl (for example trifluoromethyl). Usually R^8 will be H.

R is halo, especially chloro or fluoro, and R^2 is NR^3R^4. In the case of pyrido[2,3-b]pyrazine ring systems, the more active compounds are those where R^2 is NR^3R^4. R^3 is typically C_{1-8} alkyl (for example ethyl, *n*-propyl, *n*-butyl, *sec*-butyl (the S- or R-isomer or the racemate) and *tert*-butyl), halo(C_{1-8})alkyl (for example 2,2,2-trifluoroethyl, 2,2,2-trifluoro-1-methylethyl (the S- or R-isomer or the racemate), 3,3,3-trifluoropropyl and 4,4,4-trifluorobutyl), hydroxy(C_{1-8})alkyl (for example hydroxyethyl), C_{1-4} alkoxy(C_{1-8})alkyl (for example methoxymethyl and methoxy-*iso*-butyl), C_{1-4} alkoxyhalo(C_{1-8})alkyl (for example 2-methoxy-2-trifluromethylethyl), tri(C_{1-4})alkylsilyl(C_{1-6})alkyl (for example trimethylsilylmethyl), C_{1-4} alkylcarbonyl(C_{1-8})alkyl (for example 1-acetylethyl and 1-*tert*-butylcarbonylethyl), C_{1-4} alkylcarbonylhalo(C_{1-8})alkyl (for example 1-acetyl-2,2,2-trifluoroethyl), phenyl($_{1-4}$)alkyl (for example benzyl), C_{2-8} alkenyl (for example allyl and methylallyl), halo(C_{2-8})alkenyl (for example 3-methyl-4,4-difluorobut-3-enyl), C_{2-8} alkynyl (for example propargyl), C_{3-8} cycloalkyl (for example cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl) optionally substituted with chloro, fluoro or methyl, C_{3-8} cycloalkyl(C_{1-4})alkyl (for example cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl and cyclohexylmethyl), phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo (typically fluoro, chloro or bromo), C_{1-4} alkyl (typically methyl), halo(C_{1-4})alkyl (typically trifluoromethyl), C_{1-4} alkoxy (typically methoxy) and halo(C_{1-4})alkoxy (typically trifluoromethoxy). R^4 is typically H, C_{1-4} alkyl (for example ethyl and *n*-propyl), halo(C_{1-4})alkyl (for example 2,2,2-trifluoroethyl) or amino. Alternatively R^3 and R^4 together form a C_{4-6} alkylene chain optionally substituted with methyl, for example 3-methylpentylene, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

Typically R^1 is phenyl optionally substituted with from one to five halogen atoms, particularly fluorine and chlorine atoms and especially fluorine atoms or with from one to

three substituents selected from halo (for example fluoro and chloro), C_{1-4} alkyl (for example methyl), halo(C_{1-4})alkyl (for example trifluoromethyl), C_{1-4} alkoxy (for example methoxy) or halo(C_{1-4})alkoxy (for example trifluoromethoxy). Examples are 2,6-difluorophenyl, 2-fluoro-6-chlorophenyl, 2,5,6-trifluorophenyl, 2,4,6-trifluorophenyl, 2,6-difluoro-4-methoxyphenyl, pentafluorophenyl, 2-fluorophenyl, 2,3,5,6-tetrafluorophenyl, 2-chloro-4,6-difluorophenyl, 2-chlorophenyl, 2,6-dichlorophenyl, 2,4-dichlorophenyl, 2,4,6-trichlorophenyl, 2,3,6-trichlorophenyl, pentachlorophenyl, 2-fluoro-4,6-dichlorophenyl, 4-fluoro-2,6-dichlorophenyl, 2-bromophenyl, 2-fluoro-6-bromophenyl, 2-bromo-4,6-difluorophenyl, 2-fluoro-6-methylphenyl, 2-chloro-6-methylphenyl, 2-methoxyphenyl, 2,6-dimethoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-trifluoromethylphenyl, 2-fluoro-6-trifluoromethylphenyl, 2,6-di-(trifluoromethyl)phenyl, 2-chloro-6-trifluoromethylphenyl, 2,4-difluoro-6-trifluoromethylphenyl, 2,4-difluoro-6-methoxyphenyl and 2,4-difluoro-6-methylphenyl.

Also of particular interest are compounds where R^1 is pyridyl optionally substituted with from one to four halogen atoms or with from one to three substituents selected from halo (for example fluoro and chloro), C_{1-4} alkyl (for example methyl), halo(C_{1-4})alkyl (for example trifluoromethyl), C_{1-4} alkoxy (for example methoxy) or halo(C_{1-4})alkoxy (for example trifluoromethoxy). Examples are 2,4-difluoropyrid-3-yl, 3,5-difluoropyrid-4-yl, tetrafluoropyrid-4-yl, 3-fluoropyrid-2-yl, 4-fluoropyrid-3-yl, 3-fluoropyrid-4-yl, 2-fluoropyrid-3-yl, 2,4,6-trifluoropyrid-3-yl, 3,5-difluoropyrid-2-yl, 2,6-difluoropyrid-3-yl, 2,4-difluoro-6-methoxypyrid-3-yl, 2-fluoro-4-chloropyrid-3-yl, 3-fluoro-5-chloropyrid-4-yl, 2-chloro-4-fluoropyrid-3-yl, 2,4-dichloropyrid-3-yl, 3-chloropyrid-2-yl I, 4-chloropyrid-3-yl, 3-chloropyrid-4-yl, 2-chloropyrid-3-yl, 3-trifluoromethylpyrid-2-yl, 4-trifluoromethylpyrid-3-yl, 3,5-dichloropyrid-2-yl, 4,6-dichloropyrid-3-yl, 3-trifluoromethylpyrid-4-yl, 2-trifluoromethylpyrid-3-yl, 2-fluoro-4-trifluoromethylpyrid-3-yl, 3-fluoro-5-trifluoromethylpyrid-4-yl, 4-fluoro-2-trifluoromethylpyrid-3-yl, 2,6-dichloropyrid-3-yl, 3,5-dichloropyrid-4-yl, 3-chloro-6-trifluoromethylpyrid-2-yl, 3-fluoro-6-trifluoromethylpyrid-2-yl, pyrid-2-yl, pyrid-3-yl and pyrid-4-yl.

Also of particular interest are compounds where R^1 is 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo (for example fluoro and chloro), C_{1-4} alkyl (for example methyl), halo(C_{1-4})alkyl (for example trifluoromethyl), C_{1-4} alkoxy (for example methoxy) or halo(C_{1-4})alkoxy (for example trifluoromethoxy). Examples are 3-fluorothien-2-yl,

3-chlorothien-2-yl, 2,4-difluorothien-3-yl, 2,4-dichlorothien-3-yl and 2,4,5-trichlorothien-3-yl.

Examples of other values of R^1 of especial interest are unsubstituted piperidino and morpholino, 2-methylpiperidino, 2,6-dimethylpiperidino and 2,6-dimethylmorpholino.

In one aspect the invention provides a compound of the general formula (1) wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is halo, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C_{1-4})alkyl, aryl(C_{1-4})alkoxy, heteroaryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkoxy, aryl(C_{1-4})alkylthio, heteroaryl(C_{1-4})alkylthio, morpholino, piperidino or pyrrolidino;

R^2 is NR^3R^4;

R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6, provided that not both R^3 and R^4 are H or NR^5R^6, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and

any of the foregoing aryl, heteroaryl, aryloxy or heteroaryl groups being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl,

C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'''R'''', -NHCOR''', -NHCONR'''R'''', -CONR'''R'''', -SO_2R''', -OSO_2R''', -COR''', -CR'''=NR'''' or -N=CR'''R'''', in which R''' and R'''' are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.

Of particular interest are compounds where W and Z are both N and X and Y are both CH.

The invention includes a compound of the general formula (1) as defined immediately above except that: C_7 alkylene and C_{3-7} alkenylene are excluded as chains formed by R^3 and R^4; the C_{3-6} chain that R^3 and R^4 may form may only be optionally substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R^3 and R^4 may form; tri(C_{1-4})alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

In another aspect the invention provides a compound of the general formula (1) wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is halo, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C_{1-4})alkyl, aryl(C_{1-4})alkoxy, heteroaryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkoxy, aryl(C_{1-4})alkylthio, heteroaryl(C_{1-4})alkylthio, morpholino, piperidino or pyrrolidino;

R^2 is NR^3R^4;

R^3 is C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and

R^4 is H, C_{1-4} alkyl or amino, or

R^3 and R^4 together form a C_{4-6} alkylene chain optionally substituted with C_{1-4} alkyl or C_{1-4} alkoxy, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or

piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring;
any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,
any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and
any of the foregoing aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'"R"", -NHCOR'", -NHCONR'"R"", -CONR'"R"", -SO_2R'", -OSO_2R'", -COR'", -CR'"=NR"" or -N=CR'"R"", in which R'" and R"" are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.
Of particular interest are compounds where W and Z are both N and X and Y are both CH.

The invention includes a compound of the general formula (1) as defined immediately above except that: the C_{4-6} chain that R^3 and R^4 may form may only be optionally substituted with methyl; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R^3 and R^4 may form; tri(C_{1-4})alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

In yet another aspect the invention provides a compound of the general formula (1) wherein
W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;
R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;
R is halo;
R^1 is optionally substituted phenyl;
R^2 is NR^3R^4;
R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6, provided

that not both R^3 and R^4 are H or NR^5R^6, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and

any of the foregoing aryl or heteroaryl groups or moieties, including the phenyl group of R^1, being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'"R"", -NHCOR'", -NHCONR'"R"", -CONR'"R"", $-SO_2R'"$, $-OSO_2R'"$, -COR'", -CR'"=NR"" or -N=CR'"R"", in which R'" and R"" are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy. Of particular interest are compounds where W and Z are both N and X and Y are both CH.

The invention includes a compound of the general formula (1) as defined immediately above except that: C_{1-8} alkoxy and C_{1-8} alkylthio are excluded as values of R and R^2; C_7 alkylene and C_{3-7} alkenylene are excluded as chains formed by R^3 and R^4; the C_{3-6} chain that R^3 and R^4 may form may only be optionally substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R^3 and R^4 may form; tri(C_{1-4})alkylsilyl is excluded as a substituent

of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and the morpholine ring that R^3 and R^4 may form is unsubstituted.

In still yet another aspect the invention provides a compound of the general formula (1) wherein W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo(e.g. fluoro, chloro or bromo), C_{1-4} alkyl (e.g. methyl), C_{1-4} alkoxy (e.g. methoxy) or halo(C_{1-4})alkyl (e.g. trifluoromethyl);

R is halo (e.g. fluoro, chloro or bromo);

R^1 is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4}) alkoxy, pyridyl optionally substituted with from one to four halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, or piperidino or morpholino both optionally substituted with one or two methyl groups;

R^2 is NR^3R^4;

R^3 is C_{1-8} alkyl, halo(C_{1-8})alkyl, hydroxy(C_{1-8})alkyl, C_{1-4} alkoxy(C_{1-8})alkyl, C_{1-4} alkoxyhalo-(C_{1-8})alkyl, tri(C_{1-4})alkylsilyl(C_{1-6})alkyl, C_{1-4} alkylcarbonyl(C_{1-8})alkyl, C_{1-4} alkylcarbonyl-halo(C_{1-8})alkyl, phenyl($_{1-4}$)alkyl, C_{2-8} alkenyl, halo(C_{2-8})alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl optionally substituted with chloro, fluoro or methyl, C_{3-8} cycloalkyl(C_{1-4})alkyl, phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and

R^4 is H, C_{1-4} alkyl, halo(C_{1-4})alkyl or amino, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with methyl, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

Of particular interest are compounds where W and Z are both N and X and Y are both CH.

In still yet another aspect the invention provides a compound of the general formula (1) wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4}) alkoxy;

R^2 is NR^3R^4;

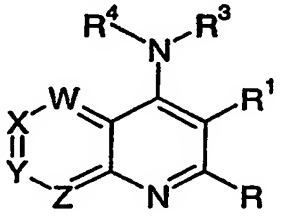
R^3 is C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and

R^4 is H, C_{1-4} alkyl or amino, or R^3 and R^4 together form a C_{4-6} alkylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine ring.

Of particular interest are compounds where W and Z are both N and X and Y are both CH.

Compounds that form part of the invention are illustrated in Tables 1 to 127 below. Characterising data are given later in the Examples and in Table 133.

In Table 1 the compounds have the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R^1 is 2,4,6-trifluorophenyl and R^3 and R^4 are as shown in the table.



(1A)

Table 1

Cmpd No	R^3	R^4
1	C_2H_5	H
2	*n*-C_3H_7	H
3	*i*-C_3H_7	H
4	*n*-C_4H_9	H
5	*t*-C_4H_9	H
6	CH_2=$CHCH_2$	H
7	CH_2=$C(CH_3)CH_2$	H
8	CF_3CH_2	H

Cmpd No	R^3	R^4
9	$CF_3CH_2CH_2$	H
10	$CF_3CH_2CH_2CH_2$	H
11	$CF_3(CH_3)CH$	H
12	(S)-$CF_3(CH_3)CH$	H
13	(R)-$CF_3(CH_3)CH$	H
14	cyclo-C_3H_5	H
15	cyclo-C_4H_7	H
16	cyclo-C_5H_9	H

Cmpd No	R^3	R^4
17	cyclo-C_6H_{11}	H
18	cyclo-$C_3H_5CH_2$	H
19	cyclo-$C_4H_7CH_2$	H
20	$-(CH_2)_2O(CH_2)_2-$	
21	cyclo-$C_6H_{11}CH_2$	H
22	$-(CH_2)_2CH(CH_3)(CH_2)_2-$	
23	$CH_3CH_2(CH_3)CH$	H
24	(S)-$CH_3CH_2(CH_3)CH$	H
25	(R)-$CH_3CH_2(CH_3)CH$	H
26	C_2H_5	C_2H_5
27	*n*-C_3H_7	*n*-C_3H_7
28	$CH_2=C(CH_3)CH_2$	C_2H_5
29	CF_3CH_2	C_2H_5
30	C_2H_5	NH_2
31	*n*-C_3H_7	NH_2
32	*i*-C_3H_7	NH_2
33	*n*-C_4H_9	NH_2
34	$CH_2=CHCH_2$	NH_2
35	$CH_2=C(CH_3)CH_2$	NH_2
36	$CF_2=CFCH_2CH_2$	NH_2
37	CF_3CH_2	NH_2
38	$CF_3CH_2CH_2$	NH_2
39	$CF_3CH_2CH_2CH_2$	NH_2
40	4-*t*-C_4H_9-C_6H_4NH	H
41	4-F-C_6H_4NH	H
42	C_6H_5NH	H
43	4-CH_3-C_6H_4NH	H
44	4-Br-C_6H_4NH	H
45	2-F-C_6H_4NH	H
46	3,4-Cl_2-C_6H_3NH	H
47	3-CF_3-C_6H_4NH	H
48	3,5-Cl_2-C_6H_3NH	H
49	4-CF_3O-C_6H_5NH	H
50	2-CF_3-C_6H_4NH	H
51	4-CF_3-C_6H_4NH	H
52	2-Br-C_6H_4NH	H
53	2-Cl-C_6H_4NH	H

Cmpd No	R^3	R^4
54	2-CH_3-4-Cl-C_6H_3NH	H
55	2-CH_3-5-F-C_6H_3NH	H
56	3-Cl-C_6H_4NH	H
57	CH_3	H
58	$(CH_3)_2CHCH_2$	H
59	$(CH_3)_3CCH_2$	H
60	$(CH_3)_3C(CH_3)CH$	H
61	$CH_3CH_2(CH_3)_2C$	H
62	$CH_3CH_2(CF_3)CH$	H
63	(S)-$CH_3CH_2(CF_3)CH$	H
64	(R)-$CH_3CH_2(CF_3)CH$	H
65	$CH_3CH_2(CH_3CH_2)CH$	H
66	$(CH_3)_2CH(CH_3CH_2)CH$	H
67	$(CH_3)_2CH(CH_3)CH$	H
68	$(CH_3)_2CH(CF_3)CH$	H
69	(S)-$(CH_3)_2CH(CF_3)CH$	H
70	(R)-$(CH_3)_2CH(CF_3)CH$	H
71	$HC=C(CH_3)CH_2$	H
72	$CH_2=CH(CH_3CH_2)CH$	H
73	$CH_3CH_2CH_2(CH_3)CH$	H
74	$CH_3CH_2CH_2(CF_3)CH$	H
75	(S)-$CH_3CH_2CH_2(CF_3)CH$	H
76	(R)-$CH_3CH_2CH_2(CF_3)CH$	H
77	$CH_3CH_2CH_2(CH_3)_2C$	H
78	$CH_3CH_2(CH_3)CHCH_2$	H
79	$(CH_3)_2CHCH_2CH_2$	H
80	$(CH_3)_3CCH_2CH_2$	H
81	$CH_3CH_2(CH_3)CH(CH_3)$-CH	H
82	$CH_3CH_2(CH_3)CH(CF_3)$-CH	H
83	(S)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	H
84	(R)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	H
85	$CH_3(CH_3)CHCH_2(CH_3)$-CH	H
86	$CH_3(CH_3)CHCH_2(CF_3)$-CH	H
87	(S)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	H

Cmpd No	R^3	R^4
88	(R)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	H
89	$(CH_3)_2CH(CH_3)CH$-$(CH_3)CH_2$	H
90	$(CH_3)_3CCH_2(CH_3)CH$	H
91	*E*-$CH_3CH{=}CH(CH_3)CH$	H
92	*E*-$CH_3CH{=}CH(CH_3CH_2)$-CH	H
93	$CH_3CH_2CH_2(CH_3CH_2)$-CH	H
94	$CH_3CH_2(CH_3CH_2)$-$CHCH_2$	H
95	$CF_2{=}CFCH_2CH_2$	H
96	$CF_3CH_2(CH_3)CHCH_2$	H
97	$CF_3CF_2CH_2CH_2$	H
98	$CF_3CF_2CF_2CH_2$	H
99	$CF_2{=}C(CH_3)CH_2CH_2$	H
100	$CH_3CH_2CH_2CH_2CH_2$	H
101	$CH_3CH_2CH_2CH_2$-$(CH_3)CH$	H
102	$CH_3CH_2CH_2(CH_3)$-$CHCH_2$	H
103	$CH_3CH_2(CH_3)CHCH_2$-CH_2	H
104	$CH_3CH_2CH_2(CH_3)CH$-$(CH_3)CH$	H
105	$CH_3CH_2(CH_3)CHCH_2$-$(CH_3)CH$	H
106	$HOCH_2CH_2$	H
107	$CH_3OCH_2CH_2$	H
108	$CH_3OCH_2(CH_3)CH$	H
109	$CH_3OCH_2(CF_3)CH$	H
110	$CH_3OCH_2(CH_3)_2C$	H
111	$CH_3O(CH_3)CHCH_2$	H
112	$CH_3O(CH_3)CH(CH_3)CH$	H
113	$HC{\equiv}CCH_2$	H
114	$CH_3C{\equiv}CCH_2$	H
115	$HC{\equiv}CCH_2CH_2$	H
116	$HOCH_2CH_2CH_2$	H
117	$CH_3OCH_2CH_2CH_2$	H
118	$(CH_3)_3SiCH_2$	H
119	$C_6H_5CH_2$	H
120	$C_6H_5(CH_3)CH$	H

Cmpd No	R^3	R^4
121	4-F-$C_6H_4CH_2$	H
122	4-Cl-$C_6H_4CH_2$	H
123	4-F-$C_6H_5(CH_3)CH$	H
124	4-Cl-$C_6H_5(CH_3)CH$	H
125	$C_6H_5CH_2CH_2$	H
126	4-F-$C_6H_5CH_2CH_2$	H
127	1-piperidino	H
128	1-pyrrolidino	H
129	cyclo-$C_5H_9CH_2$	H
130	Bicyclo[2.2.1]hept-2-yl	H
131	1-CH_3-cyclopropyl	H
132	*cis*-2-CH_3-cyclopropyl	H
133	*trans*-2-CH_3-cyclopropyl	H
134	2,2-$(CH_3)_2$-cyclopropyl	H
135	1-CH_3-cyclobutyl	H
136	*cis*-2-CH_3-cyclobutyl	H
137	*trans*-2-CH_3-cyclobutyl	H
138	*cis*-3-CH_3-cyclobutyl	H
139	*trans*-3-CH_3-cyclobutyl	H
140	2,2-$(CH_3)_2$-cyclobutyl	H
141	3,3-$(CH_3)_2$-cyclobutyl	H
142	1-CH_3-cyclopentyl	H
143	*cis*-2-CH_3-cyclopentyl	H
144	*trans*-2-CH_3-cyclopentyl	H
145	*cis*-3-CH_3-cyclopentyl	H
146	*trans*-3-CH_3-cyclopentyl	H
147	2,2-$(CH_3)_2$-cyclopentyl	H
148	3,3-$(CH_3)_2$-cyclopentyl	H
149	1-CH_3-cyclohexyl	H
150	*cis*-2-CH_3-cyclohexyl	H
151	*trans*-2-CH_3-cyclohexyl	H
152	*cis*-3-CH_3-cyclohexyl	H
153	*trans*-3-CH_3-cyclohexyl	H
154	2,2-$(CH_3)_2$-cyclohexyl	H
155	3,3-$(CH_3)_2$-cyclohexyl	H
156	*cis*-4-CH_3-cyclohexyl	H
157	*trans*-4-CH_3-cyclohexyl	H

Cmpd No	R^3	R^4
158	4,4-$(CH_3)_2$-cyclohexyl	H
159	4-$(CH_3)_3C$-cyclohexyl	H
160	-$(CH_2)_3$-	
161	-$(CH_2)_4$-	
162	-$(CH_2)_5$-	
163	-$(CH_2)_6$-	
164	-$(CH_2)_2(CH_3)_2C(CH_2)_2$-	
165	-$(CH_3)CH(CH_2)_2$-	
166	-$(CH_3)CH(CH_2)_3$-	
167	-$(CH_3)CH(CH_2)_4$-	
168	-$(CH_3)CH(CH_2)_5$-	
169	-$CH_2CH=CH(CH_2)_2$-	
170	-$(CH_2)_2NH(CH_2)_2$-	
171	-$(CH_2)_2NCH_3(CH_2)_2$-	
172	-$(CH_2)_2S(CH_2)_2$-	
173	-$(CH_2)_2SO(CH_2)_2$-	
174	-$(CH_2)_2SO_2(CH_2)_2$-	
175	-$CH_2(CH_3)CHO(CH_3)CHCH_2$-	
176	C_2H_5	CH_3
177	*n*-C_3H_7	CH_3
178	*i*-C_3H_7	CH_3
179	*n*-C_4H_9	CH_3
180	*t*-C_4H_9	CH_3
181	$CH_2=CHCH_2$	CH_3
182	$CH_2=C(CH_3)CH_2$	CH_3
183	CF_3CH_2	CH_3
184	$CF_3CH_2CH_2$	CH_3
185	$CF_3CH_2CH_2CH_2$	CH_3
186	$CF_3(CH_3)CH$	CH_3
187	(S)-$CF_3(CH_3)CH$	CH_3
188	(R)-$CF_3(CH_3)CH$	CH_3
189	cyclo-C_3H_5	CH_3
190	cyclo-C_4H_7	CH_3
191	cyclo-C_5H_9	CH_3
192	cyclo-C_6H_{11}	CH_3
193	cyclo-$C_3H_5CH_2$	CH_3
194	cyclo-$C_4H_7CH_2$	CH_3

Cmpd No	R^3	R^4
195	cyclo-$C_6H_{11}CH_2$	CH_3
196	$CH_3CH_2(CH_3)CH$	CH_3
197	(S)-$CH_3CH_2(CH_3)CH$	CH_3
198	(R)-$CH_3CH_2(CH_3)CH$	CH_3
199	cyclo-C_7H_{13}	CH_3
200	$CH_2=C(CH_3)CH_2$	CH_3
201	CF_3CH_2	CH_3
202	4-*t*-C_4H_9-C_6H_4NH	CH_3
203	4-F-C_6H_4NH	CH_3
204	C_6H_5NH	CH_3
205	4-CH_3-C_6H_4NH	CH_3
206	4-Br-C_6H_4NH	CH_3
207	2-F-C_6H_4NH	CH_3
208	3,4-Cl_2-C_6H_3NH	CH_3
209	3-CF_3-C_6H_4NH	CH_3
210	3,5-Cl_2-C_6H_3NH	CH_3
211	4-CF_3O-C_6H_5NH	CH_3
212	2-CF_3-C_6H_4NH	CH_3
213	4-CF_3-C_6H_4NH	CH_3
214	2-Br-C_6H_4NH	CH_3
215	2-Cl-C_6H_4NH	CH_3
216	2-CH_3-4-Cl-C_6H_3NH	CH_3
217	2-CH_3-5-F-C_6H_3NH	CH_3
218	3-Cl-C_6H_4NH	CH_3
219	CH_3	CH_3
220	$(CH_3)_2CHCH_2$	CH_3
221	$(CH_3)_3CCH_2$	CH_3
222	$(CH_3)_3C(CH_3)CH$	CH_3
223	$CH_3CH_2(CH_3)_2C$	CH_3
224	$CH_3CH_2(CF_3)CH$	CH_3
225	(S)-$CH_3CH_2(CF_3)CH$	CH_3
226	(R)-$CH_3CH_2(CF_3)CH$	CH_3
227	$CH_3CH_2(CH_3CH_2)CH$	CH_3
228	$(CH_3)_2CH(CH_3CH_2)CH$	CH_3
229	$(CH_3)_2CH(CH_3)CH$	CH_3
230	$(CH_3)_2CH(CF_3)CH$	CH_3
231	(S)-$(CH_3)_2CH(CF_3)CH$	CH_3

Cmpd No	R^3	R^4
232	(R)-$(CH_3)_2CH(CF_3)CH$	CH_3
233	$HC{=}C(CH_3)CH_2$	CH_3
234	$CH_2{=}CH(CH_3CH_2)CH$	CH_3
235	$CH_3CH_2CH_2(CH_3)CH$	CH_3
236	$CH_3CH_2CH_2(CF_3)CH$	CH_3
237	(S)-$CH_3CH_2CH_2(CF_3)CH$	CH_3
238	(R)-$CH_3CH_2CH_2(CF_3)CH$	CH_3
239	$CH_3CH_2CH_2(CH_3)_2C$	CH_3
240	$CH_3CH_2(CH_3)CHCH_2$	CH_3
241	$(CH_3)_2CHCH_2CH_2$	CH_3
242	$(CH_3)_3CCH_2CH_2$	CH_3
243	$CH_3CH_2(CH_3)CH(CH_3)$-CH	CH_3
244	$CH_3CH_2(CH_3)CH(CF_3)$-CH	CH_3
245	(S)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	CH_3
246	(R)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	CH_3
247	$CH_3(CH_3)CHCH_2$-$(CH_3)CH$	CH_3
248	$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	CH_3
249	(S)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	CH_3
250	(R)-$CH_3(CH_3)$ HCH_2-$(CF_3)CH$	CH_3
251	$(CH_3)_2CH(CH_3)CH(CH_3)$-CH_2	CH_3
252	$(CH_3)_3CCH_2(CH_3)CH$	CH_3
253	*E*-$CH_3CH{=}CH(CH_3)CH$	CH_3
254	*E*-$CH_3CH{=}CH(CH_3CH_2)$-CH	CH_3
255	$CH_3CH_2CH_2(CH_3CH_2)$-CH	CH_3
256	$CH_3CH_2(CH_3CH_2)$-$CHCH_2$	CH_3
257	$CF_2{=}CFCH_2CH_2$	CH_3
258	$CF_3CH_2(CH_3)CHCH_2$	CH_3
259	$CF_3CF_2CH_2CH_2$	CH_3
260	$CF_3CF_2CF_2CH_2$	CH_3
261	$CF_2{=}C(CH_3)CH_2CH_2$	CH_3
262	$CH_3CH_2CH_2CH_2CH_2$	CH_3
263	$CH_3CH_2CH_2CH_2(CH_3)$-CH	CH_3

Cmpd No	R^3	R^4
264	$CH_3CH_2CH_2(CH_3)$-$CHCH_2$	CH_3
265	$CH_3CH_2(CH_3)CHCH_2$-CH_2	CH_3
266	$CH_3CH_2CH_2(CH_3)CH$-$(CH_3)CH$	CH_3
267	$CH_3CH_2(CH_3)CHCH_2$-$(CH_3)CH$	CH_3
268	$HOCH_2CH_2$	CH_3
269	$CH_3OCH_2CH_2$	CH_3
270	$CH_3OCH_2(CH_3)CH$	CH_3
271	$CH_3OCH_2(CF_3)CH$	CH_3
272	$CH_3OCH_2(CH_3)_2C$	CH_3
273	$CH_3O(CH_3)CHCH_2$	CH_3
274	$CH_3O(CH_3)CH(CH_3)CH$	CH_3
275	$HC{\equiv}CCH_2$	CH_3
276	$CH_3C{\equiv}CCH_2$	CH_3
277	$HC{\equiv}CCH_2CH_2$	CH_3
278	$HOCH_2CH_2CH_2$	CH_3
279	$CH_3OCH_2CH_2CH_2$	CH_3
280	$(CH_3)_3SiCH_2$	CH_3
281	$C_6H_5CH_2$	CH_3
282	$C_6H_5(CH_3)CH$	CH_3
283	4-F-$C_6H_4CH_2$	H
284	4-Cl-$C_6H_4CH_2$	CH_3
285	4-F-$C_6H_5(CH_3)CH$	CH_3
286	4-Cl-$C_6H_5(CH_3)CH$	CH_3
287	$C_6H_5CH_2CH_2$	CH_3
288	4-F-$C_6H_5CH_2CH_2$	CH_3
289	1-piperidino	CH_3
290	1-pyrrolidino	CH_3
291	cyclo-$C_5H_9CH_2$	CH_3
292	bicyclo[2.2.1]hept-2-yl	CH_3
293	1-CH_3-cyclopropyl	CH_3
294	*cis*-2-CH_3-cyclopropyl	CH_3
295	*trans*-2-CH_3-cyclopropyl	CH_3
296	2,2-$(CH_3)_2$-cyclopropyl	CH_3
297	1-CH_3-cyclobutyl	CH_3
298	*cis*-2-CH_3-cyclobutyl	CH_3

Cmpd No	R^3	R^4
299	*trans*-2-CH_3-cyclobutyl	CH_3
300	*cis*-3-CH_3-cyclobutyl	CH_3
301	*trans*-3-CH_3-cyclobutyl	CH_3
302	2,2-$(CH_3)_2$-cyclobutyl	CH_3
303	3,3-$(CH_3)_2$-cyclobutyl	CH_3
304	1-CH_3-cyclopentyl	CH_3
305	*cis*-2-CH_3-cyclopentyl	CH_3
306	*trans*-2-CH_3-cyclopentyl	CH_3
307	*cis*-3-CH_3-cyclopentyl	CH_3
308	*trans*-3-CH_3-cyclopentyl	CH_3
309	2,2-$(CH_3)_2$-cyclopentyl	CH_3
310	3,3-$(CH_3)_2$-cyclopentyl	CH_3
311	1-CH_3-cyclohexyl	CH_3
312	*cis*-2-CH_3-cyclohexyl	CH_3
313	*trans*-2-CH_3-cyclohexyl	CH_3
314	*cis*-3-CH_3-cyclohexyl	CH_3
315	*trans*-3-CH_3-cyclohexyl	CH_3
316	2,2-$(CH_3)_2$-cyclohexyl	CH_3
317	3,3-$(CH_3)_2$-cyclohexyl	CH_3
318	*cis*-4-CH_3-cyclohexyl	CH_3
319	*trans*-4-CH_3-cyclohexyl	CH_3
320	4,4-$(CH_3)_2$-cyclohexyl	CH_3
321	4-$(CH_3)_3C$-cyclohexyl	CH_3
322	*n*-C_3H_7	C_2H_5
323	*i*-C_3H_7	C_2H_5
324	*n*-C_4H_9	C_2H_5
325	*t*-C_4H_9	C_2H_5
326	CH_2=$CHCH_2$	C_2H_5
327	$CF_3CH_2CH_2$	C_2H_5
328	$CF_3CH_2CH_2CH_2$	C_2H_5
329	$CF_3(CH_3)CH$	C_2H_5
330	(S)-$CF_3(CH_3)CH$	C_2H_5
331	(R)-$CF_3(CH_3)CH$	C_2H_5
332	cyclo-C_3H_5	C_2H_5
333	cyclo-C_4H_7	C_2H_5
334	cyclo-C_5H_9	C_2H_5
335	cyclo-C_6H_{11}	C_2H_5

Cmpd No	R^3	R^4
336	cyclo-$C_3H_5CH_2$	C_2H_5
337	cyclo-$C_4H_7CH_2$	C_2H_5
338	cyclo-$C_6H_{11}CH_2$	C_2H_5
339	$CH_3CH_2(CH_3)CH$	C_2H_5
340	(S)-$CH_3CH_2(CH_3)CH$	C_2H_5
341	(R)-$CH_3CH_2(CH_3)CH$	C_2H_5
342	cyclo-C_7H_{13}	C_2H_5
343	4-*t*-C_4H_9-C_6H_4NH	C_2H_5
344	4-F-C_6H_4NH	C_2H_5
345	C_6H_5NH	C_2H_5
346	4-CH_3-C_6H_4NH	C_2H_5
347	4-Br-C_6H_4NH	C_2H_5
348	2-F-C_6H_4NH	C_2H_5
349	3,4-Cl_2-C_6H_3NH	C_2H_5
350	3-CF_3-C_6H_4NH	C_2H_5
351	3,5-Cl_2-C_6H_3NH	C_2H_5
352	4-CF_3O-C_6H_5NH	C_2H_5
353	2-CF_3-C_6H_4NH	C_2H_5
354	4-CF_3-C_6H_4NH	C_2H_5
355	2-Br-C_6H_4NH	C_2H_5
356	2-Cl-C_6H_4NH	C_2H_5
357	2-CH_3-4-Cl-C_6H_3NH	C_2H_5
358	2-CH_3-5-F-C_6H_3NH	C_2H_5
359	3-Cl-C_6H_4NH	C_2H_5
360	$(CH_3)_2CHCH_2$	C_2H_5
361	$(CH_3)_3CCH_2$	C_2H_5
362	$(CH_3)_3C(CH_3)CH$	C_2H_5
363	$CH_3CH_2(CH_3)_2C$	C_2H_5
364	$CH_3CH_2(CF_3)CH$	C_2H_5
365	(S)-$CH_3CH_2(CF_3)CH$	C_2H_5
366	(R)-$CH_3CH_2(CF_3)CH$	C_2H_5
367	$CH_3CH_2(CH_3CH_2)CH$	C_2H_5
368	$(CH_3)_2CH(CH_3CH_2)CH$	C_2H_5
369	$(CH_3)_2CH(CH_3)CH$	C_2H_5
370	$(CH_3)_2CH(CF_3)CH$	C_2H_5
371	(S)-$(CH_3)_2CH(CF_3)CH$	C_2H_5
372	(R)-$(CH_3)_2CH(CF_3)CH$	C_2H_5

Cmpd No	R^3	R^4
373	$HC{=}C(CH_3)CH_2$	C_2H_5
374	$CH_2{=}CH(CH_3CH_2)CH$	C_2H_5
375	$CH_3CH_2CH_2(CH_3)CH$	C_2H_5
376	$CH_3CH_2CH_2(CF_3)CH$	C_2H_5
377	(S)-$CH_3CH_2CH_2(CF_3)CH$	C_2H_5
378	(R)-$CH_3CH_2CH_2(CF_3)CH$	C_2H_5
379	$CH_3CH_2CH_2(CH_3)_2C$	C_2H_5
380	$CH_3CH_2(CH_3)CHCH_2$	C_2H_5
381	$(CH_3)_2CHCH_2CH_2$	C_2H_5
382	$(CH_3)_3CCH_2CH_2$	C_2H_5
383	$CH_3CH_2(CH_3)CH(CH_3)$-CH	C_2H_5
384	$CH_3CH_2(CH_3)CH(CF_3)$-CH	C_2H_5
385	(S)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	C_2H_5
386	(R)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	C_2H_5
387	$CH_3(CH_3)CHCH_2(CH_3)$-CH	C_2H_5
388	$CH_3(CH_3)CHCH_2(CF_3)$-CH	C_2H_5
389	(S)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	C_2H_5
390	(R)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	C_2H_5
391	$(CH_3)_2CH(CH_3)CH$-$(CH_3)CH_2$	C_2H_5
392	$(CH_3)_3CCH_2(CH_3)CH$	C_2H_5
393	*E*-$CH_3CH{=}CH(CH_3)CH$	C_2H_5
394	*E*-C $H_3CH{=}CH$-$(CH_3CH_2)CH$	C_2H_5
395	$CH_3CH_2CH_2(CH_3CH_2)$-CH	C_2H_5
396	$CH_3CH_2(CH_3CH_2)CH$-CH_2	C_2H_5
397	$CF_2{=}CFCH_2CH_2$	C_2H_5
398	$CF_3CH_2(CH_3)CHCH_2$	C_2H_5
399	$CF_3CF_2CH_2CH_2$	C_2H_5
400	$CF_3CF_2CF_2CH_2$	C_2H_5
401	$CF_2{=}C(CH_3)CH_2CH_2$	C_2H_5
402	$CH_3CH_2CH_2CH_2CH_2$	C_2H_5
403	$CH_3CH_2CH_2CH_2(CH_3)$-CH	C_2H_5
404	$CH_3CH_2CH_2(CH_3)CH$-CH_2	C_2H_5

Cmpd No	R^3	R^4
405	$CH_3CH_2(CH_3)CHCH_2$-CH_2	C_2H_5
406	$CH_3CH_2CH_2(CH_3)CH$-$(CH_3)CH$	C_2H_5
407	$CH_3CH_2(CH_3)CHCH_2$-$(CH_3)CH$	C_2H_5
408	$HOCH_2CH_2$	C_2H_5
409	$CH_3OCH_2CH_2$	C_2H_5
410	$CH_3OCH_2(CH_3)CH$	C_2H_5
411	$CH_3OCH_2(CF_3)CH$	C_2H_5
412	$CH_3OCH_2(CH_3)_2C$	C_2H_5
413	$CH_3O(CH_3)CHCH_2$	C_2H_5
414	$CH_3O(CH_3)CH(CH_3)CH$	C_2H_5
415	$HC{\equiv}CCH_2$	C_2H_5
416	$CH_3C{\equiv}CCH_2$	C_2H_5
417	$HC{\equiv}CCH_2CH_2$	C_2H_5
418	$HOCH_2CH_2CH_2$	C_2H_5
419	$CH_3OCH_2CH_2CH_2$	C_2H_5
420	$(CH_3)_3SiCH_2$	C_2H_5
421	$C_6H_5CH_2$	C_2H_5
422	$C_6H_5(CH_3)CH$	C_2H_5
423	4-F-$C_6H_4CH_2$	C_2H_5
424	4-Cl-$C_6H_4CH_2$	C_2H_5
425	4-F-$C_6H_5(CH_3)CH$	C_2H_5
426	4-Cl-$C_6H_5(CH_3)CH$	C_2H_5
427	$C_6H_5CH_2CH_2$	C_2H_5
428	4-F-$C_6H_5CH_2CH_2$	C_2H_5
429	1-piperidino	C_2H_5
430	1-pyrrolidino	C_2H_5
431	cyclo-$C_5H_9CH_2$	C_2H_5
432	Bicyclo[2.2.1]hept-2-yl	C_2H_5
433	1-CH_3-cyclopropyl	C_2H_5
434	*cis*-2-CH_3-cyclopropyl	C_2H_5
435	*trans*-2-CH_3-cyclopropyl	C_2H_5
436	2,2-$(CH_3)_2$-cyclopropyl	C_2H_5
437	1-CH_3-cyclobutyl	C_2H_5
438	*cis*-2-CH_3-cyclobutyl	C_2H_5
439	*trans*-2-CH_3-cyclobutyl	C_2H_5
440	*cis*-3-CH_3-cyclobutyl	C_2H_5

Cmpd No	R^3	R^4
441	*trans*-3-CH_3-cyclobutyl	C_2H_5
442	2,2-$(CH_3)_2$-cyclobutyl	C_2H_5
443	3,3-$(CH_3)_2$-cyclobutyl	C_2H_5
444	1-CH_3-cyclopentyl	C_2H_5
445	*cis*-2-CH_3-cyclopentyl	C_2H_5
446	*trans*-2-CH_3-cyclopentyl	C_2H_5
447	*cis*-3-CH_3-cyclopentyl	C_2H_5
448	*trans*-3-CH_3-cyclopentyl	C_2H_5
449	2,2-$(CH_3)_2$-cyclopentyl	C_2H_5
450	3,3-$(CH_3)_2$-cyclopentyl	C_2H_5
451	1-CH_3-cyclohexyl	C_2H_5
452	*cis*-2-CH_3-cyclohexyl	C_2H_5
453	*trans*-2-CH_3-cyclohexyl	C_2H_5
454	*cis*-3-CH_3-cyclohexyl	C_2H_5
355	*trans*-3-CH_3-cyclohexyl	C_2H_5
456	2,2-$(CH_3)_2$-cyclohexyl	C_2H_5
457	3,3-$(CH_3)_2$-cyclohexyl	C_2H_5
458	*cis*-4-CH_3-cyclohexyl	C_2H_5
459	*trans*-4-CH_3-cyclohexyl	C_2H_5
460	4,4-$(CH_3)_2$-cyclohexyl	C_2H_5
461	4-$(CH_3)_3C$-cyclohexyl	C_2H_5
462	*n*-C_3H_7	CF_3CH_2
463	*i*-C_3H_7	CF_3CH_2
464	*n*-C_4H_9	CF_3CH_2
465	*t*-C_4H_9	CF_3CH_2
466	CH_2=$CHCH_2$	CF_3CH_2
467	CH_2=$C(CH_3)CH_2$	CF_3CH_2
468	CF_3CH_2	CF_3CH_2
469	$CF_3CH_2CH_2$	CF_3CH_2
470	$CF_3CH_2CH_2CH_2$	CF_3CH_2
471	$CF_3(CH_3)CH$	CF_3CH_2
472	(S)-$CF_3(CH_3)CH$	CF_3CH_2
473	(R)-$CF_3(CH_3)CH$	CF_3CH_2
474	cyclo-C_3H_5	CF_3CH_2
475	cyclo-C_4H_7	CF_3CH_2
476	cyclo-C_5H_9	CF_3CH_2
477	cyclo-C_6H_{11}	CF_3CH_2

Cmpd No	R^3	R^4
478	cyclo-$C_3H_5CH_2$	CF_3CH_2
479	cyclo-$C_4H_7CH_2$	CF_3CH_2
480	cyclo-$C_6H_{11}CH_2$	CF_3CH_2
481	$CH_3CH_2(CH_3)CH$	CF_3CH_2
482	(S)-$CH_3CH_2(CH_3)CH$	CF_3CH_2
483	(R)-$CH_3CH_2(CH_3)CH$	CF_3CH_2
484	cyclo-C_7H_{13}	CF_3CH_2
485	CH_2=$C(CH_3)CH_2$	CF_3CH_2
486	CF_3CH_2	CF_3CH_2
487	4-*t*-C_4H_9-C_6H_4NH	CF_3CH_2
488	4-F-C_6H_4NH	CF_3CH_2
489	C_6H_5NH	CF_3CH_2
490	4-CH_3-C_6H_4NH	CF_3CH_2
491	4-Br-C_6H_4NH	CF_3CH_2
492	2-F-C_6H_4NH	CF_3CH_2
493	3,4-Cl_2-C_6H_3NH	CF_3CH_2
494	3-CF_3-C_6H_4NH	CF_3CH_2
495	3,5-Cl_2-C_6H_3NH	CF_3CH_2
496	4-CF_3O-C_6H_5NH	CF_3CH_2
497	2-CF_3-C_6H_4NH	CF_3CH_2
498	4-CF_3-C_6H_4NH	CF_3CH_2
499	2-Br-C_6H_4NH	CF_3CH_2
500	2-Cl-C_6H_4NH	CF_3CH_2
501	2-CH_3-4-Cl-C_6H_3NH	CF_3CH_2
502	2-CH_3-5-F-C_6H_3NH	CF_3CH_2
503	3-Cl-C_6H_4NH	CF_3CH_2
504	$(CH_3)_2CHCH_2$	CF_3CH_2
505	$(CH_3)_3CCH_2$	CF_3CH_2
506	$(CH_3)_3C(CH_3)CH$	CF_3CH_2
507	$CH_3CH_2(CH_3)_2C$	CF_3CH_2
508	$CH_3CH_2(CF_3)CH$	CF_3CH_2
509	(S)-$CH_3CH_2(CF_3)CH$	CF_3CH_2
510	(R)-$CH_3CH_2(CF_3)CH$	CF_3CH_2
511	$CH_3CH_2(CH_3CH_2)CH$	CF_3CH_2
512	$(CH_3)_2CH(CH_3CH_2)CH$	CF_3CH_2
513	$(CH_3)_2CH(CH_3)CH$	CF_3CH_2
514	$(CH_3)_2CH(CF_3)CH$	CF_3CH_2

Cmpd No	R^3	R^4
515	(S)-$(CH_3)_2CH(CF_3)CH$	CF_3CH_2
516	(R)-$(CH_3)_2CH(CF_3)CH$	CF_3CH_2
517	$HC{=}C(CH_3)CH_2$	CF_3CH_2
518	$CH_2{=}CH(CH_3CH_2)CH$	CF_3CH_2
520	$CH_3CH_2CH_2(CH_3)CH$	CF_3CH_2
521	$CH_3CH_2CH_2(CF_3)CH$	CF_3CH_2
522	(S)-$CH_3CH_2CH_2(CF_3)CH$	CF_3CH_2
523	(R)-$CH_3CH_2CH_2(CF_3)CH$	CF_3CH_2
524	$CH_3CH_2CH_2(CH_3)_2C$	CF_3CH_2
525	$CH_3CH_2(CH_3)CHCH_2$	CF_3CH_2
526	$(CH_3)_2CHCH_2CH_2$	CF_3CH_2
527	$(CH_3)_3CCH_2CH_2$	CF_3CH_2
528	$CH_3CH_2(CH_3)CH(CH_3)$-CH	CF_3CH_2
529	$CH_3CH_2(CH_3)CH(CF_3)$-CH	CF_3CH_2
530	(S)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	CF_3CH_2
531	(R)-$CH_3CH_2(CH_3)CH$-$(CF_3)CH$	CF_3CH_2
532	$CH_3(CH_3)CHCH_2(CH_3)$-CH	CF_3CH_2
533	$CH_3(CH_3)CHCH_2(CF_3)$-CH	CF_3CH_2
534	(S)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	CF_3CH_2
535	(R)-$CH_3(CH_3)CHCH_2$-$(CF_3)CH$	CF_3CH_2
536	$(CH_3)_2CH(CH_3)CH$-$(CH_3)CH_2$	CF_3CH_2
537	$(CH_3)_3CCH_2(CH_3)CH$	CF_3CH_2
538	*E*-$CH_3CH{=}CH(CH_3)CH$	CF_3CH_2
539	*E*-$CH_3CH{=}CH(CH_3CH_2)$-CH	CF_3CH_2
540	$CH_3CH_2CH_2(CH_3CH_2)$-CH	CF_3CH_2
541	$CH_3CH_2(CH_3CH_2)CH$-CH_2	CF_3CH_2
542	$CF_2{=}CFCH_2CH_2$	CF_3CH_2
543	$CF_3CH_2(CH_3)CHCH_2$	CF_3CH_2
544	$CF_3CF_2CH_2CH_2$	CF_3CH_2
545	$CF_3CF_2CF_2CH_2$	CF_3CH_2
546	$CF_2{=}C(CH_3)CH_2CH_2$	CF_3CH_2
547	$CH_3CH_2CH_2CH_2CH_2$	CF_3CH_2
548	$CH_3CH_2CH_2CH_2(CH_3)$-CH	CF_3CH_2

Cmpd No	R^3	R^4
549	$CH_3CH_2CH_2(CH_3)CH$-CH_2	CF_3CH_2
550	$CH_3CH_2(CH_3)CHCH_2$-CH_2	CF_3CH_2
551	$CH_3CH_2CH_2(CH_3)CH$-$(CH_3)CH$	CF_3CH_2
552	$CH_3CH_2(CH_3)CHCH_2$-$(CH_3)CH$	CF_3CH_2
553	$HOCH_2CH_2$	CF_3CH_2
554	$CH_3OCH_2CH_2$	CF_3CH_2
555	$CH_3OCH_2(CH_3)CH$	CF_3CH_2
556	$CH_3OCH_2(CF_3)CH$	CF_3CH_2
557	$CH_3OCH_2(CH_3)_2C$	CF_3CH_2
558	$CH_3O(CH_3)CHCH_2$	CF_3CH_2
559	$CH_3O(CH_3)CH(CH_3)CH$	CF_3CH_2
560	$HC{\equiv}CCH_2$	CF_3CH_2
561	$CH_3C{\equiv}CCH_2$	CF_3CH_2
562	$HC{\equiv}CCH_2CH_2$	CF_3CH_2
563	$HOCH_2CH_2CH_2$	CF_3CH_2
564	$CH_3OCH_2CH_2CH_2$	CF_3CH_2
565	$(CH_3)_3SiCH_2$	CF_3CH_2
566	$C_6H_5CH_2$	CF_3CH_2
567	$C_6H_5(CH_3)CH$	CF_3CH_2
568	4-F-$C_6H_4CH_2$	CF_3CH_2
569	4-Cl-$C_6H_4CH_2$	CF_3CH_2
570	4-F-$C_6H_5(CH_3)CH$	CF_3CH_2
571	4-Cl-$C_6H_5(CH_3)CH$	CF_3CH_2
572	$C_6H_5CH_2CH_2$	CF_3CH_2
573	4-F-$C_6H_5CH_2CH_2$	CF_3CH_2
574	1-piperidino	CF_3CH_2
575	1-pyrrolidino	CF_3CH_2
576	cyclo-$C_5H_9CH_2$	CF_3CH_2
577	bicyclo[2.2.1]hept-2-yl	CF_3CH_2
578	1-CH_3-cyclopropyl	CF_3CH_2
579	*cis*-2-CH_3-cyclopropyl	CF_3CH_2
580	*trans*-2-CH_3-cyclopropyl	CF_3CH_2
581	2,2-$(CH_3)_2$-cyclopropyl	CF_3CH_2
582	1-CH_3-cyclobutyl	CF_3CH_2
583	*cis*-2-CH_3-cyclobutyl	CF_3CH_2

Cmpd No	R^3	R^4
584	*trans*-2-CH_3-cyclobutyl	CF_3CH_2
585	*cis*-3-CH_3-cyclobutyl	CF_3CH_2
586	*trans*-3-CH_3-cyclobutyl	CF_3CH_2
587	2,2-$(CH_3)_2$-cyclobutyl	CF_3CH_2
588	3,3-$(CH_3)_2$-cyclobutyl	CF_3CH_2
589	1-CH_3-cyclopentyl	CF_3CH_2
590	*cis*-2-CH_3-cyclopentyl	CF_3CH_2
591	*trans*-2-CH_3-cyclopentyl	CF_3CH_2
592	*cis*-3-CH_3-cyclopentyl	CF_3CH_2
593	*trans*-3-CH_3-cyclopentyl	CF_3CH_2
594	2,2-$(CH_3)_2$-cyclopentyl	CF_3CH_2
595	3,3-$(CH_3)_2$-cyclopentyl	CF_3CH_2
596	1-CH_3-cyclohexyl	CF_3CH_2
597	*cis*-2-CH_3-cyclohexyl	CF_3CH_2
598	*trans*-2-CH_3-cyclohexyl	CF_3CH_2
599	*cis*-3-CH_3-cyclohexyl	CF_3CH_2
600	*trans*-3-CH_3-cyclohexyl	CF_3CH_2
601	2,2-$(CH_3)_2$-cyclohexyl	CF_3CH_2
602	3,3-$(CH_3)_2$-cyclohexyl	CF_3CH_2
603	*cis*-4-CH_3-cyclohexyl	CF_3CH_2
604	*trans*-4-CH_3-cyclohexyl	CF_3CH_2
605	4,4-$(CH_3)_2$-cyclohexyl	CF_3CH_2
606	4-$(CH_3)_3C$-cyclohexyl	CF_3CH_2
607	*cis*-1-CH_3-2-fluoro-cyclopropyl	H
608	*trans*-1-CH_3-2-fluoro-cyclopropyl	H
609	1-CH_3-2,2-difluoro-cyclopropyl	H
610	*cis*-1-CH_3-2-chloro-2-fluorocyclopropyl	H
611	*trans*-1-CH_3-2-chloro-2-fluorocyclopropyl	H
612	$CH_3CO(CH_3)CH$	H
613	$CH_3CH_2CO(CH_3)CH$	H
614	$(CH_3)_2CHCO(CH_3)CH$	H
615	$(CH_3)_3CCO(CH_3)CH$	H
616	$CH_3CH_2CH_2CO(CH_3)CH$	H
617	$CH_3CO(CF_3)CH$	H
618	$CH_3CH_2CO(CF_3)CH$	H
619	$CH_3CO(CH_3)_2C$	H
620	$CH_3CH_2CO(CH_3)_2C$	H
621	*cis*-1-CH_3-2-fluoro-cyclopropyl	CH_3
622	*trans*-1-CH_3-2-fluoro-cyclopropyl	CH_3
623	1-CH_3-2,2-difluoro-cyclopropyl	CH_3
624	*cis*-1-CH_3-2-chloro-2-fluorocyclopropyl	CH_3
625	*trans*-1-CH_3-2-chloro-2-fluorocyclopropyl	CH_3
626	$CH_3CO(CH_3)CH$	CH_3
627	$CH_3CH_2CO(CH_3)CH$	CH_3
628	$(CH_3)_2CHCO(CH_3)CH$	CH_3
629	$(CH_3)_3CCO(CH_3)CH$	CH_3
630	$CH_3CH_2CH_2CO(CH_3)CH$	CH_3
631	$CH_3CO(CF_3)CH$	CH_3
632	$CH_3CH_2CO(CF_3)CH$	CH_3
633	$CH_3CO(CH_3)_2C$	CH_3
634	$CH_3CH_2CO(CH_3)_2C$	CH_3
635	*cis*-1-CH_3-2-fluoro-cyclopropyl	C_2H_5
636	*trans*-1-CH_3-2-fluoro-cyclopropyl	C_2H_5
637	1-CH_3-2,2-difluoro-cyclopropyl	C_2H_5
638	*cis*-1-CH_3-2-chloro-2-fluorocyclopropyl	C_2H_5
639	*trans*-1-CH_3-2-chloro-2-fluorocyclopropyl	C_2H_5
640	$CH_3CO(CH_3)CH$	C_2H_5
641	$CH_3CH_2CO(CH_3)CH$	C_2H_5
642	$(CH_3)_2CHCO(CH_3)CH$	C_2H_5
643	$(CH_3)_3CCO(CH_3)CH$	C_2H_5
644	$CH_3CH_2CH_2CO(CH_3)CH$	C_2H_5
645	$CH_3CO(CF_3)CH$	C_2H_5
646	$CH_3CH_2CO(CF_3)CH$	C_2H_5
647	$CH_3CO(CH_3)_2C$	C_2H_5
648	$CH_3CH_2CO(CH_3)_2C$	C_2H_5
649	*cis*-1-CH_3-2-fluoro-cyclopropyl	CF_3CH_2
650	*trans*-1-CH_3-2-fluoro-cyclopropyl	CF_3CH_2
651	1-CH_3-2,2-difluoro-cyclopropyl	CF_3CH_2

Cmpd No	R^3	R^4
652	*cis*-1-CH_3-2-chloro-2-fluorocyclopropyl	CF_3CH_2
653	*trans*-1-CH_3-2-chloro-2-fluorocyclopropyl	CF_3CH_2
654	$CH_3CO(CH_3)CH$	CF_3CH_2
655	$CH_3CH_2CO(CH_3)CH$	CF_3CH_2
656	$(CH_3)_2CHCO(CH_3)CH$	CF_3CH_2

Cmpd No	R^3	R^4
657	$(CH_3)_3CCO(CH_3)CH$	CF_3CH_2
658	$CH_3CH_2CH_2CO(CH_3)CH$	CF_3CH_2
659	$CH_3CO(CF_3)CH$	CF_3CH_2
660	$CH_3CH_2CO(CF_3)CH$	CF_3CH_2
661	$CH_3CO(CH_3)_2C$	CF_3CH_2
662	$CH_3CH_2CO(CH_3)_2C$	CF_3CH_2

Table 2

Table 2 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R^1 is 2,5,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 2 is the same as compound 1 of Table 1 except that in compound 1 of Table 2, R^1 is 2,5,6-trifluorophenyl. Similarly, compounds 2 to 662 of Table 2 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 2, R^1 is 2,5,6-trifluorophenyl.

Table 3

Table 3 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R^1 is 2,3,4,5,6-pentafluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 3 is the same as compound 1 of Table 1 except that in compound 1 of Table 3, R^1 is 2,3,4,5,6-pentafluorophenyl. Similarly, compounds 2 to 662 of Table 3 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 3, R^1 is 2,3,4,5,6-pentafluorophenyl.

Table 4

Table 4 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R^1 is 2,6-difluoro-4-methoxyphenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 4 is the same as compound 1 of Table 1 except that in compound 1 of Table 4, R^1 is 2,6-difluoro-4-methoxyphenyl. Similarly, compounds 2 to 662 of Table 4 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 4, R^1 is 2,6-difluoro-4-methoxyphenyl.

Table 5

Table 5 consists of 662 compounds of the general formula (1A), where W and Z are N, X and Y are CH, R is Cl, R^1 is 2-fluoro-6-chlorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 5 is the same as compound 1 of Table 1 except that in compound 1 of Table 5, R^1 is 2-fluoro-6-chlorophenyl. Similarly, compounds

2 to 662 of Table 5 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 5, R^1 is 2-fluoro-6-chlorophenyl.

Table 11

Table 11 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R^1 is 2,4,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 11 is the same as compound 1 of Table 1 except that in compound 1 of Table 11, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 11 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 11, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 12

Table 12 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R^1 is 2,5,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 12 is the same as compound 1 of Table 2 except that in compound 1 of Table 12, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 12 are the same as compounds 2 to 662 of Table 2 except that in the compounds of Table 12, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 13

Table 13 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R^1 is 2,3,4,5,6-pentafluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 13 is the same as compound 1 of Table 3 except that in compound 1 of Table 13, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 13 are the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 13, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 14

Table 14 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R^1 is 2,6-difluoro-4-methoxyphenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 14 is the same as compound 1 of Table 4 except that in compound 1 of Table 14, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 14 are

the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 14, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 15

Table 15 consists of 662 compounds of the general formula (1A), where W and X are N and Y and Z are CH, R is Cl, R^1 is 2-fluoro-6-chlorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 15 is the same as compound 1 of Table 5 except that in compound 1 of Table 15, the compound has the general formula (1A) where W and X are N and Y and Z are CH. Similarly, compounds 2 to 662 of Table 15 are the same as compounds 2 to 662 of Table 5 except that in the compounds of Table 15, the compounds have the general formula (1A) where W and X are N and Y and Z are CH.

Table 21

Table 21 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R^1 is 2,4,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 21 is the same as compound 1 of Table 1 except that in compound 1 of Table 21, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 21 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 21, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 22

Table 22 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R^1 is 2,5,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 22 is the same as compound 1 of Table 2 except that in compound 1 of Table 22, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 22 are the same as compounds 2 to 662 of Table 2 except that in the compounds of Table 22, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 23

Table 23 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R^1 is 2,3,4,5,6-pentafluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 23 is the same as compound 1 of Table 3 except that in compound 1 of Table 23, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 23 are

the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 23, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 24

Table 24 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R^1 is 2,6-difluoro-4-methoxyphenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 24 is the same as compound 1 of Table 4 except that in compound 1 of Table 24, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 24 are the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 24, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 25

Table 25 consists of 662 compounds of the general formula (1A), where W and Z are CH and X and Y are N, R is Cl, R^1 is 2-fluoro-6-chlorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 25 is the same as compound 1 of Table 5 except that in compound 1 of Table 25, the compound has the general formula (1A) where W and Z are CH and X and Y are N. Similarly, compounds 2 to 662 of Table 25 are the same as compounds 2 to 662 of Table 5 except that in the compounds of Table 25, the compounds have the general formula (1A) where W and Z are CH and X and Y are N.

Table 26

Table 26 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R^1 is 2,4,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 26 is the same as compound 1 of Table 1 except that in compound 1 of Table 26, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 26 are the same as compounds 2 to 662 of Table 1 except that in the compounds of Table 26, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 27

Table 27 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R^1 is 2,5,6-trifluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 27 is the same as compound 1 of Table 2 except that in compound 1 of Table 27, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 27 are the same as

compounds 2 to 662 of Table 2 except that in the compounds of Table 27, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 28

Table 28 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R^1 is 2,3,4,5,6-pentafluorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 28 is the same as compound 1 of Table 3 except that in compound 1 of Table 28, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 28 are the same as compounds 2 to 662 of Table 3 except that in the compounds of Table 28, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 29

Table 29 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R^1 is 2,6-difluoro-4-methoxyphenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 29 is the same as compound 1 of Table 4 except that in compound 1 of Table 29, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 29 are the same as compounds 2 to 662 of Table 4 except that in the compounds of Table 29, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 30

Table 30 consists of 662 compounds of the general formula (1A), where W and X are CH and Y and Z are N, R is Cl, R^1 is 2-fluoro-6-chlorophenyl, and the values of R^3 and R^4 are as listed in Table 1. Thus, compound 1 of Table 30 is the same as compound 1 of Table 5 except that in compound 1 of Table 30, the compound has the general formula (1A) where W and X are CH and Y and Z are N. Similarly, compounds 2 to 662 of Table 30 are the same as compounds 2 to 662 of Table 5 except that in the compounds of Table 30, the compounds have the general formula (1A) where W and X are CH and Y and Z are N.

Table 31

Table 31 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 31 R^1 is 2,6-difluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 32

Table 32 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 32 R^1 is 2-fluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 33

Table 33 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 33 R^1 is 2,3,5,6-tetrafluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 34

Table 34 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 34 R^1 is 2-chloro-4,6-difluorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 35

Table 35 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 35 R^1 is 2-chlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 36

Table 36 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the

same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 36 R^1 is 2,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 37

Table 37 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 37 R^1 is 2,4-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 38

Table 38 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 38 R^1 is 2,4,6-trichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 39

Table 39 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 39 R^1 is 2,3,6-trichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 40

Table 40 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 40 R^1 is pentachlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 41

Table 41 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 41 R^1 is 2-fluoro-4,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 42

Table 42 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 42 R^1 is 4-fluoro-2,6-dichlorophenyl instead of 2-fluoro-6-chlorophenyl.

Table 43

Table 43 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 43 R^1 is 2-bromophenyl instead of 2-fluoro-6-chlorophenyl.

Table 44

Table 44 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 44 R^1 is 2-fluoro-6-bromophenyl instead of 2-fluoro-6-chlorophenyl.

Table 45

Table 45 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same

as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 45 R^1 is 2-bromo-4,6-difluorophenyl instead of 2-fluoro-6-chloro-phenyl.

Table 46

Table 46 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 46 R^1 is 2-fluoro-6-methylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 47

Table 47 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 47 R^1 is 2-chloro-6-methylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 48

Table 48 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 48 R^1 is 2-methoxyphenyl instead of 2-fluoro-6-chlorophenyl.

Table 49

Table 49 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 49 R^1 is 2,6-dimethoxyphenyl instead of 2-fluoro-6-chlorophenyl.

Table 50

Table 50 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 50 R^1 is 2-fluoro-6-methoxyphenyl instead of 2-fluoro-6-chlorophenyl.

Table 51

Table 51 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 51 R^1 is 2-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 52

Table 52 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 52 R^1 is 2-fluoro-6-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 53

Table 53 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 53 R^1 is 2,6-di-(trifluoromethyl)phenyl instead of 2-fluoro-6-chlorophenyl.

Table 54

Table 54 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same

as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 54 R^1 is 2-chloro-6-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 55

Table 55 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 55 R^1 is 2,4-difluoro-6-trifluoromethylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 56

Table 56 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 56 R^1 is 2,4-difluoro-6-methoxyphenyl instead of 2-fluoro-6-chlorophenyl.

Table 57

Table 57 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 57 R^1 is 2,4-difluoro-6-methylphenyl instead of 2-fluoro-6-chlorophenyl.

Table 58

Table 58 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the

same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 58 R^1 is 2,4-difluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 59

Table 59 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 59 R^1 is 3,5-difluoropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 60

Table 60 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 60 R^1 is tetrafluoropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 61

Table 61 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 61 R^1 is 3-fluoropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 62

Table 62 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 62 R^1 is 4-fluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 63

Table 63 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 63 R^1 is 3-fluoropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 64

Table 64 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 64 R^1 is 2-fluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 65

Table 65 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 65 R^1 is 2,4,6-trifluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 66

Table 66 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 66 R^1 is 3,5-difluoropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 67

Table 67 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are

exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 67 R^1 is 2,6-difluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 68

Table 68 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 68 R^1 is 2,4-difluoro-6-methoxypyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 69

Table 69 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 69 R^1 is 2-fluoro-4-chloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 70

Table 70 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 70 R^1 is 3-fluoro-5-chloropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 71

Table 71 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 71 R^1 is 2-chloro-4-fluoropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 72

Table 72 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 72 R^1 is 2,4-dichloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 73

Table 73 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 73 R^1 is 3-chloropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 74

Table 74 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 74 R^1 is 4-chloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 75

Table 75 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 75 R^1 is 3-chloropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 76

Table 76 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are

exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 76 R^1 is 2-chloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 77

Table 77 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 77 R^1 is 3-trifluoromethylpyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 78

Table 78 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 78 R^1 is 4-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 79

Table 79 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 79 R^1 is 3,5-dichloropyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 80

Table 80 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 80 R^1 is 4,6-dichloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 81

Table 81 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same

as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 81 R^1 is 3-trifluoromethylpyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 82

Table 82 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 82 R^1 is 2-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 83

Table 83 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 83 R^1 is 2-fluoro-4-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 84

Table 84 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 84 R^1 is 3-fluoro-5-trifluoromethylpyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 85

Table 85 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the

compounds of Table 85 R^1 is 4-fluoro-2-trifluoromethylpyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 86

Table 86 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 86 R^1 is 2,6-dichloropyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 87

Table 87 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 87 R^1 is 3,5-dichloropyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 88

Table 88 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 88 R^1 is 3-chloro-6-trifluoromethylpyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 89

Table 89 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 89 R^1 is 3-fluoro-6-trifluoromethylpyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 90

Table 90 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 90 R^1 is pyrid-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 91

Table 91 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 91 R^1 is pyrid-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 92

Table 92 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 92 R^1 is pyrid-4-yl instead of 2-fluoro-6-chlorophenyl.

Table 93

Table 93 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 93 R^1 is 3-fluorothien-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 94

Table 94 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are

exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 94 R^1 is 3-chlorothien-2-yl instead of 2-fluoro-6-chlorophenyl.

Table 95

Table 95 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 95 R^1 is 2,4-difluorothien-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 96

Table 96 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 96 R^1 is 2,4-dichlorothien-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 97

Table 97 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table R^1 is 2,4,5-trichlorothien-3-yl instead of 2-fluoro-6-chlorophenyl.

Table 98

Table 98 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 98 R^1 is piperidino instead of 2-fluoro-6-chlorophenyl.

Table 99

Table 99 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same

as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 99 R^1 is 2-methylpiperidino instead of 2-fluoro-6-chlorophenyl.

Table 100

Table 100 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 100 R^1 is 2,6-dimethylpiperidino instead of 2-fluoro-6-chlorophenyl.

Table 101

Table 101 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 101 R^1 is morpholino instead of 2-fluoro-6-chlorophenyl.

Table 102

Table 102 consists of 2648 compounds. Compounds 1 to 662 are exactly the same as compounds 1 to 662 of Table 5 respectively, compounds 1325 to 1986 are exactly the same as compounds 1 to 662 of Table 15 respectively, compounds 2649 to 3310 are exactly the same as compounds 1 to 662 of Table 25 respectively, and compounds 3311 to 3972 are exactly the same as compounds 1 to 662 of Table 30 respectively, except that in all of the compounds of Table 102 R^1 is 2,6-dimethylmorpholino instead of 2-fluoro-6-chlorophenyl.

Table 103

Table 103 consists of 201,248 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of Table 103 is the same as compound 1 of Table 1, compound 663 of Table 103 is the same as compound 1 of Table 2, compound 19,861 of Table 103 is the same as compound 1 of Table 31, compound 305,844 of Table 103 is the same as compound 3,972 of Table 102) except that in all of the compounds of Table 103 R is F instead of Cl.

Table 104

Table 104 consists of 201,248 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 102 (thus, for example, compound 1 of Table 104 is the same as compound 1 of Table 1, compound 663 of Table 104 is the same as compound 1 of Table 2, compound 19,861 of Table 104 is the same as compound 1 of Table 31, compound 305,844 of Table 104 is the same as compound 3,972 of Table 102) except that in all of the compounds of Table 104 R is Br instead of Cl.

Table 109

Table 109 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 109 is the same as compound 1 of Table 1, compound 663 of Table 109 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 109 X is CF instead of CH.

Table 110

Table 110 consists of 3310c compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 110 is the same as compound 1 of Table 1, compound 663 of Table 110 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 110 X is CCl instead of CH.

Table 111

Table 111 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 111 is the same as compound 1 of Table 1, compound 663 of Table 111 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 111 X is CBr instead of CH.

Table 112

Table 112 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 112 is the same as compound 1 of Table 1, compound 663 of Table 112 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 112 X is CCH_3 instead of CH.

Table 113

Table 113 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 113 is the same as compound 1 of Table 1, compound 663 of Table 113 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 113 Y is CF instead of CH.

Table 114

Table 114 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 114 is the same as compound 1 of Table 1, compound 663 of Table 114 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 114 Y is CCl instead of CH.

Table 115

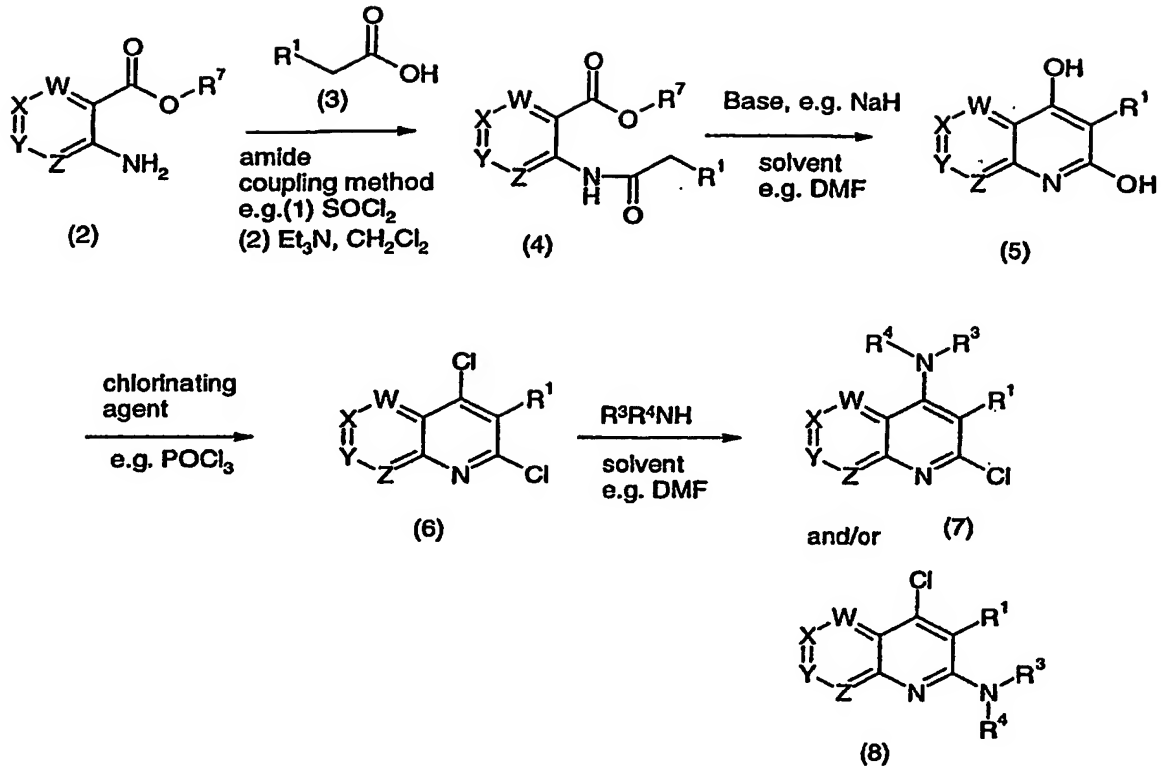
Table 115 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 115 is the same as compound 1 of Table 1, compound 663 of Table 115 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 115 Y is CBr instead of CH.

Table 116

Table 116 consists of 3310 compounds. Each of these compounds is exactly the same as the corresponding compound in Tables 1 to 5 (thus, for example, compound 1 of Table 116 is the same as compound 1 of Table 1, compound 663 of Table 116 is the same as compound 1 of Table 2, etc.) except that in all of the compounds of Table 116 Y is CCH_3 instead of CH.

Compounds of formula (7) or (8), which are examples of compounds of general formula (1) where one of R and R^2 is NR^3R^4, can be made as shown in Scheme 1, in which W, X, Y, Z, R^1, R^3 and R^4 have the meanings given above and R^7 is C_{1-4} alkyl.

Scheme 1



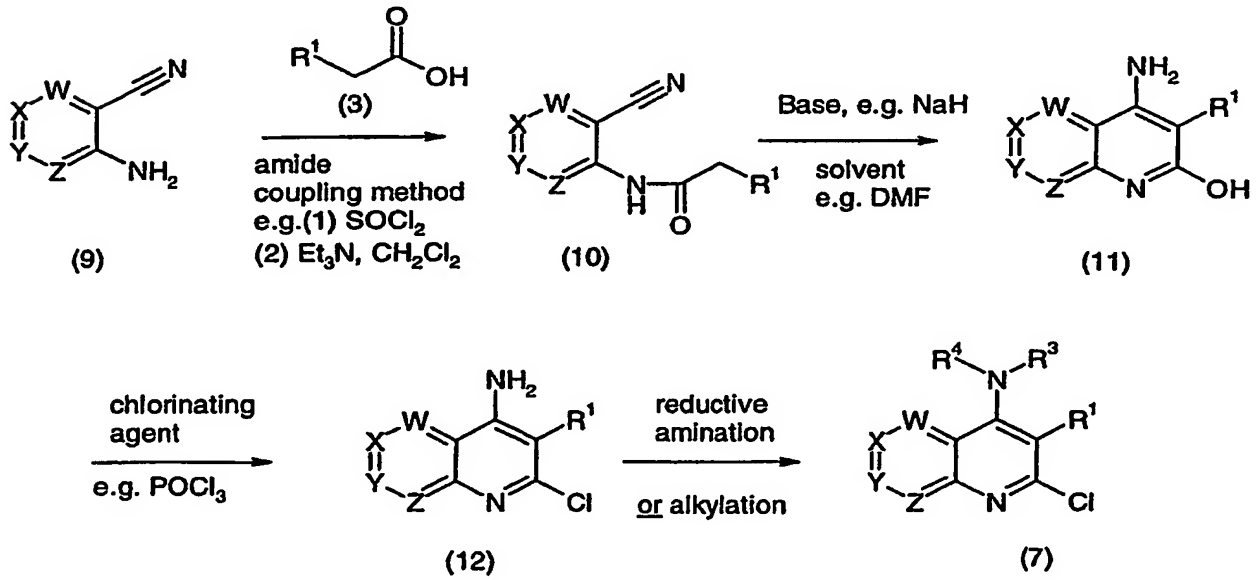
Compounds of general formula (4) can be prepared from compounds of general formula (2), which are either commercially available or made by methods known in the literature, by reaction with acids of general formula (3), using standard coupling methods, for example by conversion to the acid chloride using a chlorinating agent such as thionyl chloride, followed by reaction of the resultant acid chloride optionally in the presence of a base such as triethylamine, in a suitable solvent such as dichloromethane or toluene. Compounds of general formula (5) can be prepared by treating compounds of general formula (4) with a base such as sodium hydride, optionally in the presence of a Lewis acid such as magnesium oxide, in a suitable solvent such as *N,N*-dimethylformamide (DMF) or toluene, at between room temperature and 150°C, but preferably at 60-90°C. Compounds of general formula (6) can be prepared by reaction of compounds of general formula (5) with a chlorination reagent such as phosphorus oxychloride, either neat or in a suitable solvent such as toluene, at between 50 and 150°C, but preferably between 80 and 110°C, or in a microwave reactor at between 150 and 300°C, but preferably between 200 and 250°C. Compounds of formula (7) and (8) can be prepared by reaction of compounds of general formula (6) with an amine R^3R^4NH, either neat, or in a suitable solvent such as DMF,

between room temperature and 150°C, but preferably between 50 and 80°C. If compounds (7) and (8) are produced as a mixture they can be separated by suitable means such as crystallisation or chromatography under normal or reverse phase conditions.

Compounds of the general formulae (5), (6), (7) and (8) may be derivatised, via the chloro or hydroxy substituents, using routine chemical techniques to form other compounds of the general formula (1). Alternatively, other compounds of the general formula (1) may be prepared using a similar methodology to that described for preparing the compounds (5) to (8) and employing preparative techniques known from the chemical literature.

Compounds of formula (7) can also be made as shown in Scheme 2.

Scheme 2

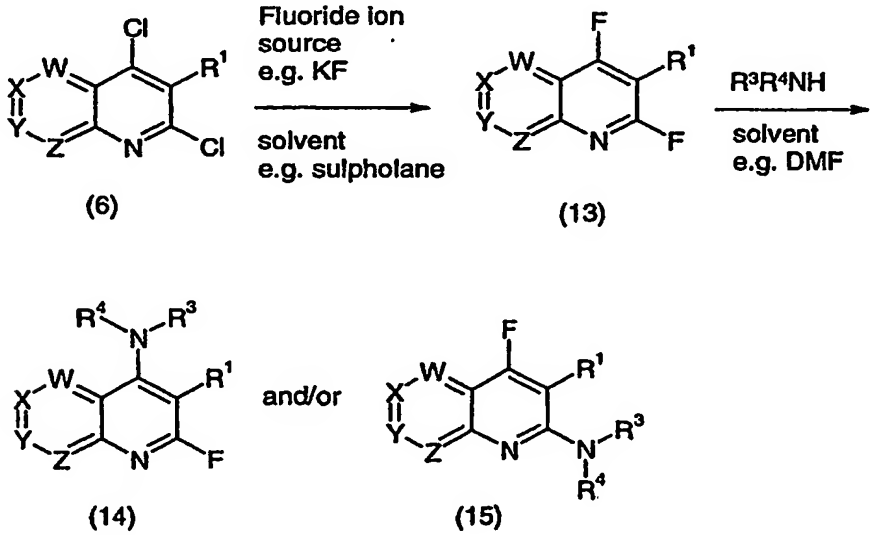


Compounds of general formula (10) can be prepared from compounds of general formula (9), which are either commercially available or made by methods known in the literature, by reaction with acids of general formula (3), using standard coupling methods, for example by conversion to the acid chloride using a chlorinating agent such as thionyl chloride, followed by reaction of the resultant acid chloride optionally in the presence of a base such as triethylamine, in a suitable solvent such as dichloromethane or toluene. Compounds of general formula (11) can be prepared by treating compounds of general formula (10) with a base such as sodium hydride, optionally in the presence of a Lewis acid such as magnesium oxide, in a suitable solvent such as *N,N*-dimethylformamide (DMF) or toluene, at between room temperature and 150°C, but preferably at 60-90°C. Compounds of

general formula (12) can be prepared by reaction of compounds of general formula (11) with a chlorination reagent such as phosphorus oxychloride, either neat or in a suitable solvent such as toluene, at between 50 and 150°C, but preferably between 80 and 110°C, or in a microwave reactor at between 150 and 300°C, but preferably between 200 and 250°C.

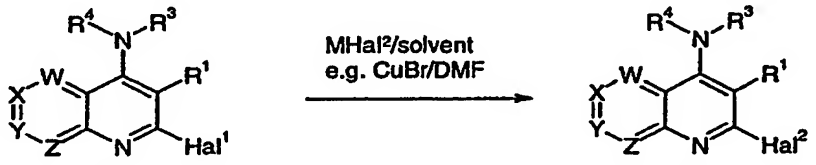
Compounds of formula (7) can be prepared from compounds of formula (12) by reductive amination, for example by reaction with a ketone or aldehyde in a suitable solvent such as ethanol or toluene, at between room temperature and reflux, optionally in the presence of an acid catalyst such as para-toluenesulphonic acid or a drying agent such as molecular sieves, followed by treatment with a suitable reducing agent such as sodium borohydride, at between –20°C and 40°C, but preferably at room temperature. The aldehyde or ketone is chosen so that the desired groups R^3 and R^4 are formed after reduction of the product of reaction with the amine (12). For example if compounds of formula (12) are reacted with one equivalent of propionaldehyde and then sodium borohydride, compounds of formula (7) where R^3 is *n*-propyl, and R^4 is hydrogen are formed. If required, the reaction can be repeated with a different aldehyde or ketone. For example, if acetone is used for the second reaction, then compounds of formula (7) where R^3 is *n*-propyl and R^4 is *iso*-propyl, are formed. Alternatively compounds of formula (7) can be formed from compounds of formula (12) by alkylation with a group R^3LG, by treatment with a suitable base such as sodium hydride in a solvent such as DMF, or a base such as potassium carbonate in a solvent such as acetone or DMF, at between –78°C and 100°C, but preferably between room temperature and 60°C, followed by treatment with R^4LG in a second step under the same conditions if required.

Scheme 3



Compounds of formula (13) can be prepared as shown in Scheme 3 from compounds of formula (6) by reaction with a source of fluoride ion, such as potassium fluoride, in a suitable solvent such as sulpholane, at a temperature between 50°C and 200°C, but preferably at 80-150°C. Compounds of formula (14) and/or compounds of formula (15) can be prepared from difluoro compounds of formula (13) by reaction with an amine of formula R^3R^4NH in a suitable solvent such as DMF or CH_2Cl_2, at a temperature of 0°C-100°C, but preferably at room temperature.

Scheme 4

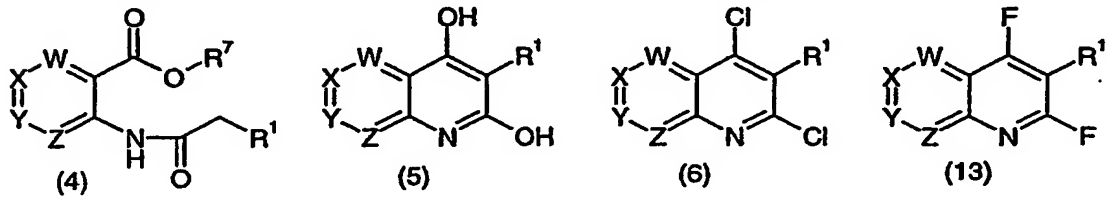


(16) (17)

Compounds of general formula (16), where Hal^1 is chlorine or fluorine, can be converted into compounds of formula (17) as shown in Scheme 4. Compounds of general formula (17) where Hal^2 is bromine or iodine can be formed by reacting compounds of general formula (16) with a metal halide, for example cuprous bromide, in a suitable solvent, for example DMF, at between room temperature and 155°C, but preferably between 70°C and 155°C.

Further assistance in the preparation of the compounds of formula (1) may be derived from the following publications: Emilio, Toja, *et. al.*, *J. Heterocyclic Chem.*, 23, 1955 (1986), H. Schäfer, *et. al.*, *J. f. prakt. Chemie*, 321(4), 695 (1970) and H. Bredereck *et. al.*, *Chem. Ber.* 96, 1868-1872 (1993).

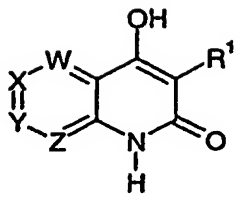
The intermediate chemicals having the general formulae (4), (5), (6) and (13):



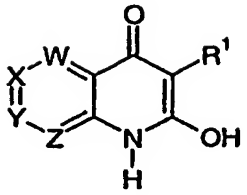
(4) (5) (6) (13)

wherein W, X, Y, Z, R^1 and R^7 are as define above, other than the compound of formula (6) wherein X and Y are N, W and Z are C-Cl and R^1 is Cl, are believed to be novel compounds and form a further part of this invention.

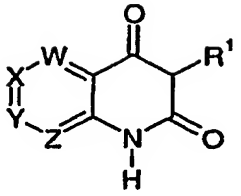
It should be noted that the intermediate of general formula (5) may exist in the tautomeric forms (a), (b) and (c) as well as in the form shown in formula (5):



(a)



(b)



(c)

The invention as defined by the general formula (5) embraces all such tautomers.

Of particular interest are the intermediates listed in Tables 128 to 132 below. In Table 128 the compounds have the general formula (4) where R^7 is methyl and W, X, Y, Z and R^1 have the values shown in the table.

Table 128

Cmpd No.	R^1	W	X	Y	Z
1	2,4,6-trifluorophenyl	N	CH	CH	N
2	2,5,6-trifluorophenyl	N	CH	CH	N
3	2,3,4,5,6-pentafluorophenyl	N	CH	CH	N
4	2,3,5,6-tetrafluorophenyl	N	CH	CH	N
5	2,6-difluoro-4-methoxyphenyl	N	CH	CH	N
6	2-fluoro-6-chlorophenyl	N	CH	CH	N
7	2,6-difluorophenyl	N	CH	CH	N
8	2,3,5,6-tetrafluorophenyl	N	CH	CH	N
9	2-fluorophenyl	N	CH	CH	N
10	2-chlorophenyl	N	CH	CH	N
11	2-bromophenyl	N	CH	CH	N
12	2,4-dichlorophenyl	N	CH	CH	N
13	2,4,6-trifluorophenyl	N	N	CH	CH
14	2,5,6-trifluorophenyl	N	N	CH	CH
15	2,3,4,5,6-pentafluorophenyl	N	N	CH	CH
16	2,3,5,6-tetrafluorophenyl	N	N	CH	CH
17	2,6-difluoro-4-methoxyphenyl	N	N	CH	CH
18	2-fluoro-6-chlorophenyl	N	N	CH	CH
19	2,6-difluorophenyl	N	N	CH	CH

20	2,3,5,6-tetrafluorophenyl	N	N	CH	CH
21	2-fluorophenyl	N	N	CH	CH
22	2-chlorophenyl	N	N	CH	CH
23	2-bromophenyl	N	N	CH	CH
24	2,4-dichlorophenyl	N	N	CH	CH
25	2,4,6-trifluorophenyl	CH	N	N	CH
26	2,5,6-trifluorophenyl	CH	N	N	CH
27	2,3,4,5,6-pentafluorophenyl	CH	N	N	CH
28	2,3,5,6-tetrafluorophenyl	CH	N	N	CH
29	2,6-difluoro-4-methoxyphenyl	CH	N	N	CH
30	2-fluoro-6-chlorophenyl	CH	N	N	CH
31	2,6-difluorophenyl	CH	N	N	CH
32	2,3,5,6-tetrafluorophenyl	CH	N	N	CH
33	2-fluorophenyl	CH	N	N	CH
34	2-chlorophenyl	CH	N	N	CH
35	2-bromophenyl	CH	N	N	CH
36	2,4-dichlorophenyl	CH	N	N	CH
37	2,4,6-trifluorophenyl	CH	CH	N	N
38	2,5,6-trifluorophenyl	CH	CH	N	N
39	2,3,4,5,6-pentafluorophenyl	CH	CH	N	N
40	2,3,5,6-tetrafluorophenyl	CH	CH	N	N
41	2,6-difluoro-4-methoxyphenyl	CH	CH	N	N
42	2-fluoro-6-chlorophenyl	CH	CH	N	N
43	2,6-difluorophenyl	CH	CH	N	N
44	2,3,5,6-tetrafluorophenyl	CH	CH	N	N
45	2-fluorophenyl	CH	CH	N	N
46	2-chlorophenyl	CH	CH	N	N
47	2-bromophenyl	CH	CH	N	N
48	2,4-dichlorophenyl	CH	CH	N	N

Table 129

Table 129 consists of 48 compounds of the general formula (5), where W, X, Y, Z and R^1 have the values given in Table 128. Thus, compound 1 of Table 129 has the same W, X, Y, Z and R^1 values as compound 1 of Table 128, etc.

Table 130

Table 130 consists of 48 compounds of the general formula (6), where W, X, Y, Z and R^1 have the values given in Table 128. Thus, compound 1 of Table 130 has the same W, X, Y, Z and R^1 values as compound 1 of Table 128, etc.

Table 131

Table 131 consists of 48 compounds of the general formula (13), where W, X, Y, Z and R^1 have the values given in Table 128. Thus, compound 1 of Table 131 has the same W, X, Y, Z and R^1 values as compound 1 of Table 128, etc.

Table 132

Table 132 consists of 48 compounds of the general formula (4), where W, X, Y, Z and R^1 have the values given in Table 128 and R^7 is ethyl. Thus, compound 1 of Table 132 is the same as compound 1 of Table 128 except that in compound 1 of Table 132, R^7 is ethyl instead of methyl. Similarly, compounds 2 to 48 of Table 132 are the same as compounds 2 to 48 of Table 128 except that in the compounds of Table 132, R^7 is ethyl.

The compounds of formula (1) are active fungicides and may be used to control one or more of the following pathogens: *Pyricularia oryzae* (*Magnaporthe grisea*) on rice and wheat and other *Pyricularia* spp. on other hosts; *Puccinia triticina* (or *recondita*), *Puccinia striiformis* and other rusts on wheat, *Puccinia hordei*, *Puccinia striiformis* and other rusts on barley, and rusts on other hosts (for example turf, rye, coffee, pears, apples, peanuts, sugar beet, vegetables and ornamental plants); *Erysiphe cichoracearum* on cucurbits (for example melon); *Blumeria* (or *Erysiphe*) *graminis* (powdery mildew) on barley, wheat, rye and turf and other powdery mildews on various hosts, such as *Sphaerotheca macularis* on hops, *Sphaerotheca fusca* (*Sphaerotheca fuliginea*) on cucurbits (for example cucumber), *Leveillula taurica* on tomatoes, aubergine and green pepper, *Podosphaera leucotricha* on apples and *Uncinula necator* on vines; *Cochliobolus* spp., *Helminthosporium* spp., *Drechslera* spp. (*Pyrenophora* spp.), *Rhynchosporium* spp., *Mycosphaerella graminicola* (*Septoria tritici*) and *Phaeosphaeria nodorum* (*Stagonospora nodorum* or *Septoria nodorum*), *Pseudocercosporella herpotrichoides* and *Gaeumannomyces graminis* on cereals (for example wheat, barley, rye), turf and other hosts; *Cercospora arachidicola* and

Cercosporidium personatum on peanuts and other *Cercospora* spp. on other hosts, for example sugar beet, bananas, soya beans and rice; *Botrytis cinerea* (grey mould) on tomatoes, strawberries, vegetables, vines and other hosts and other *Botrytis* spp. on other hosts; *Alternaria* spp. on vegetables (for example carrots), oil-seed rape, apples, tomatoes, potatoes, cereals (for example wheat) and other hosts; *Venturia* spp. (including *Venturia inaequalis* (scab)) on apples, pears, stone fruit, tree nuts and other hosts; *Cladosporium* spp. on a range of hosts including cereals (for example wheat) and tomatoes; *Monilinia* spp. on stone fruit, tree nuts and other hosts; *Didymella* spp. on tomatoes, turf, wheat, cucurbits and other hosts; *Phoma* spp. on oil-seed rape, turf, rice, potatoes, wheat and other hosts; *Aspergillus* spp. and *Aureobasidium* spp. on wheat, lumber and other hosts; *Ascochyta* spp. on peas, wheat, barley and other hosts; *Stemphylium* spp. (*Pleospora* spp.) on apples, pears, onions and other hosts; summer diseases (for example bitter rot (*Glomerella cingulata*), black rot or frogeye leaf spot (*Botryosphaeria obtusa*), Brooks fruit spot (*Mycosphaerella pomi*), Cedar apple rust (*Gymnosporangium juniperi-virginianae*), sooty blotch (*Gloeodes pomigena*), flyspeck (*Schizothyrium pomi*) and white rot (*Botryosphaeria dothidea*)) on apples and pears; *Plasmopara viticola* on vines; other downy mildews, such as *Bremia lactucae* on lettuce, *Peronospora* spp. on soybeans, tobacco, onions and other hosts, *Pseudoperonospora humuli* on hops and *Pseudoperonospora cubensis* on cucurbits; *Pythium* spp. (including *Pythium ultimum*) on turf and other hosts; *Phytophthora infestans* on potatoes and tomatoes and other *Phytophthora* spp. on vegetables, strawberries, avocado, pepper, ornamentals, tobacco, cocoa and other hosts; *Thanatephorus cucumeris* on rice and turf and other *Rhizoctonia* spp. on various hosts such as wheat and barley, peanuts, vegetables, cotton and turf; *Sclerotinia* spp. on turf, peanuts, potatoes, oil-seed rape and other hosts; *Sclerotium* spp. on turf, peanuts and other hosts; *Gibberella fujikuroi* on rice; *Colletotrichum* spp. on a range of hosts including turf, coffee and vegetables; *Laetisaria fuciformis* on turf; *Mycosphaerella* spp. on bananas, peanuts, citrus, pecans, papaya and other hosts; *Diaporthe* spp. on citrus, soybean, melon, pears, lupin and other hosts; *Elsinoe* spp. on citrus, vines, olives, pecans, roses and other hosts; *Verticillium* spp. on a range of hosts including hops, potatoes and tomatoes; *Pyrenopeziza* spp. on oil-seed rape and other hosts; *Oncobasidium theobromae* on cocoa causing vascular streak dieback; *Fusarium* spp., *Typhula* spp., *Microdochium nivale*, *Ustilago* spp., *Urocystis* spp., *Tilletia* spp. and *Claviceps purpurea* on a variety of hosts but particularly wheat, barley, turf and maize; *Ramularia* spp. on sugar beet, barley and other hosts; post-harvest diseases particularly of fruit (for example

Penicillium digitatum, *Penicillium italicum* and *Trichoderma viride* on oranges, *Colletotrichum musae* and *Gloeosporium musarum* on bananas and *Botrytis cinerea* on grapes); other pathogens on vines, notably *Eutypa lata*, *Guignardia bidwellii*, *Phellinus igniarus*, *Phomopsis viticola*, *Pseudopeziza tracheiphila* and *Stereum hirsutum*; other pathogens on trees (for example *Lophodermium seditiosum*) or lumber, notably *Cephaloascus fragrans*, *Ceratocystis* spp., *Ophiostoma piceae*, *Penicillium* spp., *Trichoderma pseudokoningii*, *Trichoderma viride*, *Trichoderma harzianum*, *Aspergillus niger*, *Leptographium lindbergi* and *Aureobasidium pullulans*; and fungal vectors of viral diseases (for example *Polymyxa graminis* on cereals as the vector of barley yellow mosaic virus (BYMV) and *Polymyxa betae* on sugar beet as the vector of rhizomania).

A compound of formula (1) may move acropetally, basipetally or locally in plant tissue to be active against one or more fungi. Moreover, a compound of formula (1) may be volatile enough to be active in the vapour phase against one or more fungi on the plant.

The invention therefore provides a method of combating or controlling phytopathogenic fungi which comprises applying a fungicidally effective amount of a compound of formula (1), or a composition containing a compound of formula (1), to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other plant growth medium, e.g. nutrient solution.

The term "plant" as used herein includes seedlings, bushes and trees. Furthermore, the fungicidal method of the invention includes protectant, curative, systemic, eradicant and antisporulant treatments.

The compounds of formula (1) are preferably used for agricultural, horticultural and turfgrass purposes in the form of a composition.

In order to apply a compound of formula (1) to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other growth medium, a compound of formula (1) is usually formulated into a composition which includes, in addition to the compound of formula (1), a suitable inert diluent or carrier and, optionally, a surface active agent (SFA). SFAs are chemicals that are able to modify the properties of an interface (for example, liquid/solid, liquid/air or liquid/liquid interfaces) by lowering the interfacial tension and thereby leading to changes in other properties (for example dispersion, emulsification and wetting). It is preferred that all compositions (both solid and liquid formulations) comprise, by weight, 0.0001 to 95%, more preferably 1 to 85%, for example 5 to 60%, of a compound of formula (1). The composition is generally used for the control of fungi such that a

compound of formula (1) is applied at a rate of from 0.1g to10kg per hectare, preferably from 1g to 6kg per hectare, more preferably from 1g to 1kg per hectare.

When used in a seed dressing, a compound of formula (1) is used at a rate of 0.0001g to 10g (for example 0.001g or 0.05g), preferably 0.005g to 10g, more preferably 0.005g to 4g, per kilogram of seed.

In another aspect the present invention provides a fungicidal composition comprising a fungicidally effective amount of a compound of formula (1) and a suitable carrier or diluent therefor.

In a still further aspect the invention provides a method of combating and controlling fungi at a locus, which comprises treating the fungi, or the locus of the fungi with a fungicidally effective amount of a composition comprising a compound of formula (1).

The compositions can be chosen from a number of formulation types, including dustable powders (DP), soluble powders (SP), water soluble granules (SG), water dispersible granules (WG), wettable powders (WP), granules (GR) (slow or fast release), soluble concentrates (SL), oil miscible liquids (OL), ultra low volume liquids (UL), emulsifiable concentrates (EC), dispersible concentrates (DC), emulsions (both oil in water (EW) and water in oil (EO)), micro-emulsions (ME), suspension concentrates (SC), aerosols, fogging/smoke formulations, capsule suspensions (CS) and seed treatment formulations. The formulation type chosen in any instance will depend upon the particular purpose envisaged and the physical, chemical and biological properties of the compound of formula (1).

Dustable powders (DP) may be prepared by mixing a compound of formula (1) with one or more solid diluents (for example natural clays, kaolin, pyrophyllite, bentonite, alumina, montmorillonite, kieselguhr, chalk, diatomaceous earths, calcium phosphates, calcium and magnesium carbonates, sulphur, lime, flours, talc and other organic and inorganic solid carriers) and mechanically grinding the mixture to a fine powder.

Soluble powders (SP) may be prepared by mixing a compound of formula (1) with one or more water-soluble inorganic salts (such as sodium bicarbonate, sodium carbonate or magnesium sulphate) or one or more water-soluble organic solids (such as a polysaccharide) and, optionally, one or more wetting agents, one or more dispersing agents or a mixture of said agents to improve water dispersibility/solubility. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water soluble granules (SG).

Wettable powders (WP) may be prepared by mixing a compound of formula (1) with one or more solid diluents or carriers, one or more wetting agents and, preferably, one or

more dispersing agents and, optionally, one or more suspending agents to facilitate the dispersion in liquids. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water dispersible granules (WG).

Granules (GR) may be formed either by granulating a mixture of a compound of formula (1) and one or more powdered solid diluents or carriers, or from pre-formed blank granules by absorbing a compound of formula (1) (or a solution thereof, in a suitable agent) in a porous granular material (such as pumice, attapulgite clays, fuller's earth, kieselguhr, diatomaceous earths or ground corn cobs) or by adsorbing a compound of formula (1) (or a solution thereof, in a suitable agent) on to a hard core material (such as sands, silicates, mineral carbonates, sulphates or phosphates) and drying if necessary. Agents which are commonly used to aid absorption or adsorption include solvents (such as aliphatic and aromatic petroleum solvents, alcohols, ethers, ketones and esters) and sticking agents (such as polyvinyl acetates, polyvinyl alcohols, dextrins, sugars and vegetable oils). One or more other additives may also be included in granules (for example an emulsifying agent, wetting agent or dispersing agent).

Dispersible Concentrates (DC) may be prepared by dissolving a compound of formula (1) in water or an organic solvent, such as a ketone, alcohol or glycol ether. These solutions may contain a surface active agent (for example to improve water dilution or prevent crystallisation in a spray tank).

Emulsifiable concentrates (EC) or oil-in-water emulsions (EW) may be prepared by dissolving a compound of formula (1) in an organic solvent (optionally containing one or more wetting agents, one or more emulsifying agents or a mixture of said agents). Suitable organic solvents for use in ECs include aromatic hydrocarbons (such as alkylbenzenes or alkylnaphthalenes, exemplified by SOLVESSO 100, SOLVESSO 150 and SOLVESSO 200; SOLVESSO is a Registered Trade Mark), ketones (such as cyclohexanone or methylcyclohexanone), alcohols (such as benzyl alcohol, furfuryl alcohol or butanol), *N*-alkylpyrrolidones (such as *N*-methylpyrrolidone or *N*-octylpyrrolidone), dimethyl amides of fatty acids (such as C_8-C_{10} fatty acid dimethylamide) and chlorinated hydrocarbons. An EC product may spontaneously emulsify on addition to water, to produce an emulsion with sufficient stability to allow spray application through appropriate equipment. Preparation of an EW involves obtaining a compound of formula (1) either as a liquid (if it is not a liquid at room temperature, it may be melted at a reasonable temperature, typically below 70°C) or in solution (by dissolving it in an appropriate solvent) and then emulsifying the resultant liquid

or solution into water containing one or more SFAs, under high shear, to produce an emulsion. Suitable solvents for use in EWs include vegetable oils, chlorinated hydrocarbons (such as chlorobenzenes), aromatic solvents (such as alkylbenzenes or alkylnaphthalenes) and other appropriate organic solvents that have a low solubility in water.

Microemulsions (ME) may be prepared by mixing water with a blend of one or more solvents with one or more SFAs, to produce spontaneously a thermodynamically stable isotropic liquid formulation. A compound of formula (1) is present initially in either the water or the solvent/SFA blend. Suitable solvents for use in MEs include those hereinbefore described for use in in ECs or in EWs. An ME may be either an oil-in-water or a water-in-oil system (which system is present may be determined by conductivity measurements) and may be suitable for mixing water-soluble and oil-soluble pesticides in the same formulation. An ME is suitable for dilution into water, either remaining as a microemulsion or forming a conventional oil-in-water emulsion.

Suspension concentrates (SC) may comprise aqueous or non-aqueous suspensions of finely divided insoluble solid particles of a compound of formula (1). SCs may be prepared by ball or bead milling the solid compound of formula (1) in a suitable medium, optionally with one or more dispersing agents, to produce a fine particle suspension of the compound. One or more wetting agents may be included in the composition and a suspending agent may be included to reduce the rate at which the particles settle. Alternatively, a compound of formula (1) may be dry milled and added to water, containing agents hereinbefore described, to produce the desired end product.

Aerosol formulations comprise a compound of formula (1) and a suitable propellant (for example *n*-butane). A compound of formula (1) may also be dissolved or dispersed in a suitable medium (for example water or a water miscible liquid, such as *n*-propanol) to provide compositions for use in non-pressurised, hand-actuated spray pumps.

A compound of formula (1) may be mixed in the dry state with a pyrotechnic mixture to form a composition suitable for generating, in an enclosed space, a smoke containing the compound.

Capsule suspensions (CS) may be prepared in a manner similar to the preparation of EW formulations but with an additional polymerisation stage such that an aqueous dispersion of oil droplets is obtained, in which each oil droplet is encapsulated by a polymeric shell and contains a compound of formula (1) and, optionally, a carrier or diluent therefor. The polymeric shell may be produced by either an interfacial polycondensation reaction or by a

coacervation procedure. The compositions may provide for controlled release of the compound of formula (1) and they may be used for seed treatment. A compound of formula (1) may also be formulated in a biodegradable polymeric matrix to provide a slow, controlled release of the compound.

A composition may include one or more additives to improve the biological performance of the composition (for example by improving wetting, retention or distribution on surfaces; resistance to rain on treated surfaces; or uptake or mobility of a compound of formula (1)). Such additives include surface active agents, spray additives based on oils, for example certain mineral oils or natural plant oils (such as soy bean and rape seed oil), and blends of these with other bio-enhancing adjuvants (ingredients which may aid or modify the action of a compound of formula (1)).

A compound of formula (1) may also be formulated for use as a seed treatment, for example as a powder composition, including a powder for dry seed treatment (DS), a water soluble powder (SS) or a water dispersible powder for slurry treatment (WS), or as a liquid composition, including a flowable concentrate (FS), a solution (LS) or a capsule suspension (CS). The preparations of DS, SS, WS, FS and LS compositions are very similar to those of, respectively, DP, SP, WP, SC and DC compositions described above. Compositions for treating seed may include an agent for assisting the adhesion of the composition to the seed (for example a mineral oil or a film-forming barrier).

Wetting agents, dispersing agents and emulsifying agents may be SFAs of the cationic, anionic, amphoteric or non-ionic type.

Suitable SFAs of the cationic type include quaternary ammonium compounds (for example cetyltrimethyl ammonium bromide), imidazolines and amine salts.

Suitable anionic SFAs include alkali metals salts of fatty acids, salts of aliphatic monoesters of sulphuric acid (for example sodium lauryl sulphate), salts of sulphonated aromatic compounds (for example sodium dodecylbenzenesulphonate, calcium dodecylbenzenesulphonate, butylnaphthalene sulphonate and mixtures of sodium di-*iso*propyl- and tri-*iso*propyl-naphthalene sulphonates), ether sulphates, alcohol ether sulphates (for example sodium laureth-3-sulphate), ether carboxylates (for example sodium laureth-3-carboxylate), phosphate esters (products from the reaction between one or more fatty alcohols and phosphoric acid (predominately mono-esters) or phosphorus pentoxide (predominately di-esters), for example the reaction between lauryl alcohol and tetraphosphoric acid; additionally these

products may be ethoxylated), sulphosuccinamates, paraffin or olefine sulphonates, taurates and lignosulphonates.

Suitable SFAs of the amphoteric type include betaines, propionates and glycinates.

Suitable SFAs of the non-ionic type include condensation products of alkylene oxides, such as ethylene oxide, propylene oxide, butylene oxide or mixtures thereof, with fatty alcohols (such as oleyl alcohol or cetyl alcohol) or with alkylphenols (such as octylphenol, nonylphenol or octylcresol); partial esters derived from long chain fatty acids or hexitol anhydrides; condensation products of said partial esters with ethylene oxide; block polymers (comprising ethylene oxide and propylene oxide); alkanolamides; simple esters (for example fatty acid polyethylene glycol esters); amine oxides (for example lauryl dimethyl amine oxide); and lecithins.

Suitable suspending agents include hydrophilic colloids (such as polysaccharides, polyvinylpyrrolidone or sodium carboxymethylcellulose) and swelling clays (such as bentonite or attapulgite).

A compound of formula (1) may be applied by any of the known means of applying fungicidal compounds. For example, it may be applied, formulated or unformulated, to any part of the plant, including the foliage, stems, branches or roots, to the seed before it is planted or to other media in which plants are growing or are to be planted (such as soil surrounding the roots, the soil generally, paddy water or hydroponic culture systems), directly or it may be sprayed on, dusted on, applied by dipping, applied as a cream or paste formulation, applied as a vapour or applied through distribution or incorporation of a composition (such as a granular composition or a composition packed in a water-soluble bag) in soil or an aqueous environment.

A compound of formula (1) may also be injected into plants or sprayed onto vegetation using electrodynamic spraying techniques or other low volume methods, or applied by land or aerial irrigation systems.

Compositions for use as aqueous preparations (aqueous solutions or dispersions) are generally supplied in the form of a concentrate containing a high proportion of the active ingredient, the concentrate being added to water before use. These concentrates, which may include DCs, SCs, ECs, EWs, MEs SGs, SPs, WPs, WGs and CSs, are often required to withstand storage for prolonged periods and, after such storage, to be capable of addition to water to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. Such aqueous preparations may

contain varying amounts of a compound of formula (1) (for example 0.0001 to 10%, by weight) depending upon the purpose for which they are to be used.

A compound of formula (1) may be used in mixtures with fertilisers (for example nitrogen-, potassium- or phosphorus-containing fertilisers). Suitable formulation types include granules of fertiliser. The mixtures suitably contain up to 25% by weight of the compound of formula (1).

The invention therefore also provides a fertiliser composition comprising a fertiliser and a compound of formula (1).

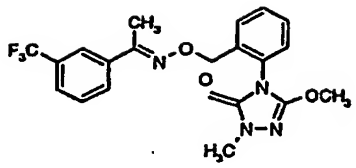
The compositions of this invention may contain other compounds having biological activity, for example micronutrients or compounds having similar or complementary fungicidal activity or which possess plant growth regulating, herbicidal, insecticidal, nematicidal or acaricidal activity.

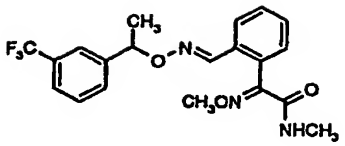
By including another fungicide, the resulting composition may have a broader spectrum of activity or a greater level of intrinsic activity than the compound of formula (1) alone. Further the other fungicide may have a synergistic effect on the fungicidal activity of the compound of formula (1).

The compound of formula (1) may be the sole active ingredient of the composition or it may be admixed with one or more additional active ingredients such as a pesticide, fungicide, synergist, herbicide or plant growth regulator where appropriate. An additional active ingredient may: provide a composition having a broader spectrum of activity or increased persistence at a locus; synergise the activity or complement the activity (for example by increasing the speed of effect or overcoming repellency) of the compound of formula (1); or help to overcome or prevent the development of resistance to individual components. The particular additional active ingredient will depend upon the intended utility of the composition.

Examples of fungicidal compounds which may be included in the composition of the invention are AC 382042 (*N*-(1-cyano-1,2-dimethylpropyl)-2-(2,4-dichlorophenoxy) propionamide), acibenzolar-S-methyl, alanycarb, aldimorph, anilazine, azaconazole, azafenidin, azoxystrobin, benalaxyl, benomyl, benthiavalicarb, biloxazol, bitertanol, blasticidin S, boscalid (new name for nicobifen), bromuconazole, bupirimate, captafol, captan, carbendazim, carbendazim chlorhydrate, carboxin, carpropamid, carvone, CGA 41396, CGA 41397, chinomethionate, chlorbenzthiazone, chlorothalonil, chlorozolinate, clozylacon, copper containing compounds such as copper oxychloride, copper oxyquinolate, copper

sulphate, copper tallate, and Bordeaux mixture, cyamidazosulfamid, cyazofamid (IKF-916), cyflufenamid, cymoxanil, cyproconazole, cyprodinil, debacarb, di-2-pyridyl disulphide 1,1'-dioxide, dichlofluanid, diclocymet, diclomezine, dicloran, diethofencarb, difenoconazole, difenzoquat, diflumetorim, *O,O*-di-*iso*-propyl-*S*-benzyl thiophosphate, dimefluazole, dimetconazole, dimethirimol, dimethomorph, dimoxystrobin, diniconazole, dinocap, dithianon, dodecyl dimethyl ammonium chloride, dodemorph, dodine, doguadine, edifenphos, epoxiconazole, ethaboxam, ethirimol, ethyl (*Z*)-*N*-benzyl-*N*([methyl(methyl-thioethylideneaminooxycarbonyl)amino]thio)-β-alaninate, etridiazole, famoxadone, fenamidone, fenarimol, fenbuconazole, fenfuram, fenhexamid, fenoxanil (AC 382042), fenpiclonil, fenpropidin, fenpropimorph, fentin acetate, fentin hydroxide, ferbam, ferimzone, fluazinam, fludioxonil, flumetover, flumorph, fluoroimide, fluoxastrobin, fluquinconazole, flusilazole, flusulfamide, flutolanil, flutriafol, folpet, fosetyl-aluminium, fuberidazole, furalaxyl, furametpyr, guazatine, hexaconazole, hydroxyisoxazole, hymexazole, imazalil, imibenconazole, iminoctadine, iminoctadine triacetate, ipconazole, iprobenfos, iprodione, iprovalicarb, isopropanyl butyl carbamate, isoprothiolane, kasugamycin, kresoxim-methyl, LY186054, LY211795, LY 248908, mancozeb, maneb, mefenoxam, mepanipyrim, mepronil, metalaxyl, metalaxyl M, metconazole, metiram, metiram-zinc, metominostrobin, metrafenone, MON65500 (*N*-allyl-4,5-dimethyl-2-trimethylsilylthiophene-3-carboxamide), myclobutanil, NTN0301, neoasozin, nickel dimethyldithiocarbamate, nitrothale-isopropyl, nuarimol, ofurace, organomercury compounds, orysastrobin, oxadixyl, oxasulfuron, oxolinic acid, oxpoconazole, oxycarboxin, pefurazoate, penconazole, pencycuron, phenazin oxide, phosphorus acids, phthalide, picoxystrobin, polyoxin D, polyram, probenazole, prochloraz, procymidone, propamocarb, propamocarb hydrochloride, propiconazole, propineb, propionic acid, proquinazid, prothioconazole, pyraclostrobin, pyrazophos, pyrifenox, pyrimethanil, pyroquilon, pyroxyfur, pyrrolnitrin, quaternary ammonium compounds, quinomethionate, quinoxyfen, quintozene, silthiofam (MON 65500), S-imazalil, simeconazole, sipconazole, sodium pentachlorophenate, spiroxamine, streptomycin, sulphur, tebuconazole, tecloftalam, tecnazene, tetraconazole, thiabendazole, thifluzamide, 2-(thiocyanomethylthio)-benzothiazole, thiophanate-methyl, thiram, tiadinil, timibenconazole, tolclofos-methyl, tolylfluanid, triadimefon, triadimenol, triazbutil, triazoxide, tricyclazole, tridemorph, trifloxystrobin, triflumizole, triforine, triticonazole, validamycin A, vapam, vinclozolin, XRD-563, zineb, ziram, zoxamide and compounds of the formulae:





The compounds of formula (1) may be mixed with soil, peat or other rooting media for the protection of plants against seed-borne, soil-borne or foliar fungal diseases.

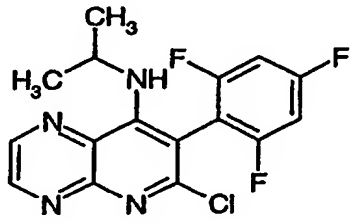
Some mixtures may comprise active ingredients, which have significantly different physical, chemical or biological properties such that they do not easily lend themselves to the same conventional formulation type. In these circumstances other formulation types may be prepared. For example, where one active ingredient is a water insoluble solid and the other a water insoluble liquid, it may nevertheless be possible to disperse each active ingredient in the same continuous aqueous phase by dispersing the solid active ingredient as a suspension (using a preparation analogous to that of an SC) but dispersing the liquid active ingredient as an emulsion (using a preparation analogous to that of an EW). The resultant composition is a suspoemulsion (SE) formulation.

The invention is illustrated by the following Examples in which the following abbreviations are used:

ml = millilitres
g = grammes
ppm = parts per million
s = singlet
d = doublet
t = triplet
q = quartet
m = multiplet
b = broad
f = fine
THF = tetrahydrofuran
DCM = dichloromethane
DMF = *N*, *N*-dimethylformamide
DMSO = dimethylsulphoxide
DMAP = 4-dimethylaminopyridine
NMR = nuclear magnetic resonance
HPLC = high performance liquid chromatography

EXAMPLE 1

This Example illustrates the preparation of [6-chloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine (Compound No. 3, Table 1).



Compound No.3, Table 1

Step 1

Methyl 2-amino-3-pyrazine carboxylate (2.2 g) was dissolved in dry DCM (20 ml) to give a cloudy pale yellow solution, and pyridine (2 ml) in dry DCM (12 ml) was added. The stirred suspension was cooled in an ice bath, and 2,4,6-trifluorophenylacetyl chloride (3.0 g) in dry DCM (13 ml) was added dropwise. The reaction gradually became a deep orange, and then went clear. It was stirred for 6 hours and stood overnight. The reaction mixture was washed with water, brine, and then dilute hydrochloric acid, and the DCM layer was dried over magnesium sulphate. The solvent was evaporated to yield an orange solid which was triturated with ether, to give methyl 2-[2,4,6-trifluorophenylacetylamino]-3-pyrazine carboxylate as a yellow solid (1.5 g).

^{1}H NMR ($CDCl_3$) δ ppm: 4.03 (s,5H), 6.74 (t,2H), 8.43 (d,1H), 8.61 (d,1H) 10.9 (s,1H).

Step 2

The product of Step 1 (3.25 g) was dissolved in DMF (10ml) and added dropwise to a stirred suspension of sodium hydride (0.60 g of an 80% dispersion in mineral oil) in DMF (80 ml). There was an immediate reaction, and the mixture was stirred at room temperature for 2 hours, and at 80°C for 8 hours. The reaction mixture was cooled and evaporated to give a yellow solid (3 g), which was then acidified with dilute hydrochloric acid. The resultant white suspension was filtered and collected, washed with ether and dried to give 6,8-dihydroxy-7-(2,4,6-trifluorophenyl)pyrido[2,3-b]pyrazine (1.8 g).

^{1}H NMR (d^6-DMSO) δ ppm: 7.25 (t,2H), 8.6 (fd,1H),8.7 (fd,1H), 12.6 (s,1H).

Step 3

The product from Step 2 (0.90 g) was added portion-wise to phosphorus oxychloride (10 ml) with stirring. The reaction was exothermic. The mixture became brown with a fine suspension, and was then refluxed for 6 hours. Excess phosphorus oxychloride was evaporated, the mixture was diluted with DCM, and then washed with water to give a black

oil, which was purified by flash column chromatography on silica gel (40-60) eluting with diethyl ether, to give 6,8-dichloro-7-(2,4,6-trifluorophenyl)pyrido[2,3-b]pyrazine as a dark oil (0.40 g).

^{1}H NMR ($CDCl_3$) δ ppm: 6.9 (t,2H), 9.1(d,1H), 9.2 (d,1H).

Alternative procedure for Step 3

Phosphorus oxychloride (20.90 g) was added over 15 minutes to a suspension of the product from Step 2 (10.0 g), in 1,2-dichloroethane (80 ml) containing DMF (5.0 g) maintained at a temperature between 79°- 81°C. Stirring was continued at this temperature for 3 hours, and the reaction was then cooled. The mixture was poured carefully into saturated sodium bicarbonate solution (500 ml) keeping the temperature below 30 °C. After stirring for 20 minutes the product was extracted with ethyl acetate, washed with water and brine and dried over sodium sulphate. The solvent was evaporated to yield a dark red oil, which was purified by flash chromatography eluting with cyclohexane:ethyl acetate, 4:1 to give 6,8-dichloro-7-(2,4,6-trifluorophenyl)pyrido[2,3-b]pyrazine as a light brown solid (7.5 g), m.p. 139-141 °C.

Step 4

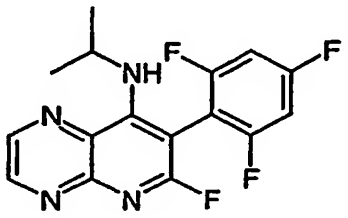
The product from Step 3 (0.20 g), isopropylamine (1.0 ml) and *N*-ethyl-di*iso*propylamine (0.20 g) were refluxed in a sealed tube at 90°C for 17 hours. The dark coloured reaction mixture was evaporated to give an oil, which was purified by flash column chromatography on silica gel (40-60) in diethyl ether.

A fraction containing a mixture of isomers (0.080 g), was obtained, and a portion of this mixture (0.020g) was purified by reverse phase HPLC on a Kromasil 100-5C18 column, eluting with methanol:water (65:35) to give [6-chloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine as a frothy solid (0.013 g).

^{1}H NMR ($CDCl_3$) δ ppm: 1.1 (d,6H), 3.26 (m,1H), 6.84 (m,2H), 6.95 (bd,1H), 8.67 (d,1H), 9.0 (d,1H).

EXAMPLE 2

This Example illustrates the preparation of [6-fluoro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine (Compound No. 3, Table 103)



Step 1

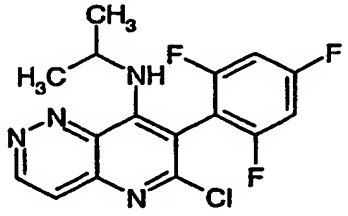
6,8-Dichloro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazine (1.25 g) and potassium fluoride (0.66 g, spray dried) in dry sulpholane (5 ml) were heated to 130 °C for 16 hours. The reaction mixture was poured into water and extracted with ethyl acetate. The extract was washed with water and brine and dried over sodium sulphate. After evaporation of the solvent, the remaining oil was purified by flash chromatography on silica gel eluting with cyclohexane:ethyl acetate, 3:1 to yield 6,8-difluoro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]-pyrazine as a slightly brownish solid (0.79 g), m.p. 120-121 °C.

Step 2

The product from Step 1 (0.30 g) was added to a suspension of isopropylamine (0.090 g), potassium carbonate (0.21 g) and a catalytic amount of DMAP in DMF (3 ml), and the mixture was stirred at room temperature for 19 hours. After addition of ethyl acetate, the mixture was washed with water and brine, dried over sodium sulphate, filtered and the solvent evaporated. The residue was purified by flash chromatography eluting with toluene:ethyl acetate, 9:1 to give [6-fluoro-7-(2,4,6-trifluorophenyl)-pyrido[2,3-b]pyrazin-8-yl]-isopropylamine as a yellow powder (0.20 g), m.p. 127-128 °C.

EXAMPLE 3

This Example illustrates the preparation of [6-chloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazin-8-yl]-isopropylamine (Compound No. 3, Table 11) .



Compound No. 3, Table 11

Step 1

A solution of 4-aminopyridazine-3-carbonitrile (0.248 g, prepared as in *J. Het. Chem.*(1970), 3, 467-473) in absolute ethanol (30 ml)was saturated with hydrogen chloride gas, the flask being cooled in an ice bath. The ice bath was then removed and the resulting solution was refluxed for 18 hours. It was then cooled, the solvent evaporated, and cold, saturated aqueous sodium bicarbonate was added. The aqueous phase was then extracted with DCM, the organic phases were combined, dried over magnesium sulphate, filtered and evaporated to give 4-aminopyridazine-3-carboxylic acid ethyl ester as a white solid (0.229g). The aqueous phase was evaporated, DCM was added, the organic phase was isolated, dried over magnesium sulphate, filtered and evaporated under *vacuo* to give further ester as a white solid (0.010 g), m.p. 149-150°C.

^{1}H NMR ($CDCl_3$) δ ppm: 1.48 (t,3H), 4.52 (q,2H), 6.73 (d,1H), 8.75 (d,1H).

Step 2

A mixture of the product from Step 1 (0.239 g) and DMAP (0.175 g) in dry toluene (1 ml) was added to 2,4,6-trifluorophenylacetyl chloride (crude product from reaction of 0.275 g 2,4,6-trifluorophenylacetic acid and oxalyl chloride) and a few drops of DMF in toluene (1 ml) at room temperature, giving a thick yellow precipitate. The stirred suspension was heated for 3 hours at reflux, becoming dark brown/green with a green precipitate. It was left to stand overnight for 18 hours. The solid was collected and washed with diethyl ether. The dark green filtrate was evaporated to give a dark green liquid which was purified by flash column chromatography on silica gel (40-60) eluting with ethyl acetate to give 4-[2-(2,4,6-trifluorophenyl)-acetylamino]-pyridazine-3-carboxylic acid ethyl ester as green/yellow oil that solidified on standing (0.307 g).

^{1}H NMR ($CDCl_3$) δ ppm: 1.50 (t,3H), 3.87 (s,2H), 4.55 (q,2H), 6.77 (t,2H), 8.78 (d,1H), 9.15 (d,1H), 11.20 (bs,1H).

Step 3

The product from Step 2 (0.307 g) and potassium carbonate (0.25 g) were stirred in dry DMF (10 ml) at 110°C for 2 hours and then cooled and stood for 18 hours. The DMF was evaporated and the resulting brown solid was triturated with diethyl ether and the organic phase decanted. The solid was dissolved in water then acidified with dilute hydrochloric acid to neutrality. Most of the aqueous phase was then evaporated, leading to precipitation of a black solid that was filtered, and the yellow/brown aqueous phase was evaporated to dryness, affording a residue that was dissolved in methanol, the insoluble inorganic salts were filtered and the organic phase was evaporated to dryness to give 7-

(2,4,6-trifluorophenyl)-5H-pyrido[3,2-c]pyridazine-6,8-dione as a light brown/beige solid (0.258 g).

^{1}H NMR (CD_3OD) δ ppm: 6.83 (2d,2H), 7.44 (d,1H), 9.00 (d,1H).

Step 4

Phosphorus oxychloride (0.048 ml) was added to the product from Step 3 (0.05 g) in 1,2-dichloroethane (2 ml) containing a catalytic amount of DMF. The suspension was stirred and refluxed for 1 hour and then stood for 18 hours, and then refluxed for a further hour and then allowed to cool. The excess phosphorus oxychloride was evaporated to give a brown oil, which was dissolved in DCM and washed with cold water. The organic layer was separated and dried over magnesium sulphate, filtered and evaporated to give a brown oil, which was purified by flash column chromatography on silica gel (40-60) eluting with diethyl ether to give 6,8-dichloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazine as a yellow oil (0.015 g).

^{1}H NMR ($CDCl_3$) δ ppm: 6.92 (m,2H), 8.11 (d,1H), 9.71 (d,1H).

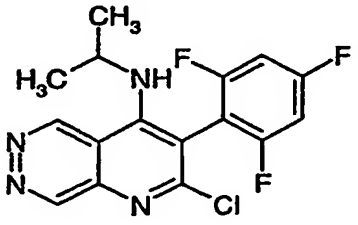
Step 5

Isopropylamine (0.5 ml) was added to the product from Step 4 (0.015 g) dissolved in DCM (1ml) containing dimethylacetamide (0.3 ml) in a sealed tube. The yellow solution became yellow/greenish. The vessel was then sealed and stirred at room temperature. The solvents were evaporated and the crude residue was purified using preparative thin layer chromatography silica gel plates eluting with ethyl acetate:hexane 1:1 to give [6-Chloro-7-(2,4,6-trifluorophenyl)-pyrido[3,2-c]pyridazin-8-yl]-isopropylamine (0.003 g).

^{1}H NMR ($CDCl_3$) δ ppm: 1.16 (d,6H), 3.41 (m,1H), 6.85 (dd,2H), 7.79 (bs,1H), 7.84 (d,1H). 9.40 (d,1H).

EXAMPLE 4

This Example illustrates the preparation of [2-chloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazin-4-yl]-isopropylamine (Compound No. 3, Table 21).



Compound No. 3, Table 21

Step 1

5-Aminopyridazine-4-carboxylic acid ethyl ester (1.26 g, prepared according to *J. Het. Chem.*, (1968), 5, 845) was dissolved in dry toluene (125 ml) at 90°C, and DMAP (0.92 g) was added. 2,4,6-Trifluorophenylacetyl chloride (1.75 g of 95% purity material) was added dropwise with stirring at 70°C, and a white solid precipitated. The reaction was stirred at reflux for 5 hours and then filtered hot. The filtrate was evaporated to give 5-[2-(2,4,6-trifluorophenyl)-acetylamino]-pyridazine-4-carboxylic acid ethyl ester as a white solid (2.6 g), m.p. 143-144°C.

^{1}H NMR ($CDCl_3$) δ ppm: 1.45 (t,3H), 3.90 (s,2H), (4.45 (q,2H), 6.75 (m,2H), 9.45 (s1H), 10.60 (s,1H), 11.1 (bs,1H).

Step 2

The product from Step 1 (2.5 g) was dissolved in dry THF (50 ml) and the flask purged with nitrogen. Sodium bis-trimethylsilylamide (22.1 ml of a 1M solution in THF) was added dropwise with stirring at 0°C. A yellow precipitate appeared, and the reaction was stirred for 3 hours at 0°C. The reaction was quenched with concentrated hydrochloric acid (5 ml) at 0°C and then poured onto ice water, extracted with DCM and dried over magnesium sulphate. The solvent was evaporated to give 3-(2,4,6-trifluorophenyl)-1*H*-pyrido[2,3-d]pyridazine-2,4-dione as a yellow solid. Further product crystallised out of the aqueous solution overnight, to give a total yield of 1.29 g, m.p. >300°C.

^{1}H NMR (d^6-DMSO) δ ppm: 7.25 (m,2H), 9.17 (s,1H), 9.47 (s,1H), 12.30 (bs,1H).

Step 3

The product from Step 2 (0.10 g) was heated to 90°C with phosphorus oxychloride (1.6 ml) with stirring. After 1 hour a clear yellow solution was obtained and the excess solvent was evaporated and ice water was added, giving a yellow solid. This was extracted with DCM, and the solution dried over magnesium sulphate and evaporated to give 2,4-dichloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazine as a yellow foamy glass (0.11 g).

^{1}H NMR ($CDCl_3$) δ ppm: 6.90 (m,2H), 9.80 (s,1H), 10.0 (s, H).

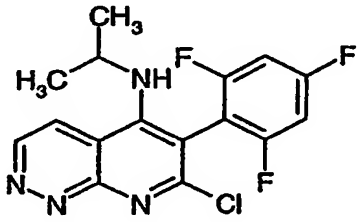
Step 4

Isopropylamine (1.5 ml) was added to the product from Step 3 (0.020 g) in DCM and the tube stoppered and the reaction stirred overnight at room temperature. The DCM was evaporated and water added to the residue, which was then extracted with DCM. The extract was dried over magnesium sulphate and evaporated to give an orange oil, which was purified by HPLC eluting with ethyl acetate:hexane 4:1 to give

[2-Chloro-3-(2,4,6-trifluorophenyl)-pyrido[2,3-d]pyridazin-4-yl]-isopropylamine (0.007 g)
^{1}H NMR ($CDCl_3$) δ ppm: 1.27 (d,6H), 4.05 (m,1H), 4.90 (bs,1H), 6.92 (m,2H), 9.55 (s,1H), 9.90 (s,1H).

EXAMPLE 5

This Example illustrates the preparation of [7-chloro-6-(2,4,6-trifluorophenyl)-pyrido[2,3-c]pyridazin-5-yl]-isopropylamine (Compound No. 3, Table 26).



Compound No. 3, Table 26

Step 1

3-Aminopyridazine-4-carboxylic acid (1.68 g, prepared as in JOC, (1985), 50, 346) was refluxed in ethanol (170 ml) with concentrated hydrochloric acid (2 ml) and *p*-toluene-sulphonyl chloride (0.1 g) for 55 hours. The solvent was evaporated and ice water added to the residue, which was then neutralised with solid sodium bicarbonate. The mixture was extracted with chloroform, insoluble material filtered, the organic extract dried over magnesium sulphate and evaporated to give 3-aminopyridazine-4-carboxylic acid ethyl ester (1.02 g) as a white solid.
^{1}H NMR ($CDCl_3$) δ ppm: 1.40 (t,3H), 4.40 (q,2H), 6.50 (bs,2H), 7.74 (d,1H), 8.72 (d,1H).

Step 2

The product from Step 1 (0.36g) was dissolved in dry toluene (25 ml) and DMAP (0.262 g) was added. A solution of 2,4,6-trifluorophenylacetyl chloride (0.45 g) in dry toluene (1 ml) was added dropwise with stirring, and a white precipitate formed. After stirring at room temperature for 10 minutes the reaction was stirred under reflux for 4.5 hours, and then allowed to stand overnight at room temperature. The white solid was filtered and washed with toluene, and the filtrate evaporated to give a brown oil, which was purified by HPLC eluting with ethyl acetate:hexane 4:1 to give 3-[2-(2,4,6-trifluorophenyl)-acetylamino]-pyridazine-4-carboxylic acid ethyl ester as a pale yellow solid (0.57 g), m.p. 135°C.
^{1}H NMR ($CDCl_3$) δ ppm: 1.40 (t,3H), 4.22 (s,2H), 4.41 (q,2H), 6.70 (m,2H), 7.94 (d,1H), 9.15 (d,1H), 10.30 (bs,1H).

Step 3

The product from Step 2 (2.0 g) was dissolved in dry THF (50 ml), and sodium bis-trimethylsilylamide (17.7 ml of a 1.0M solution in THF) was added dropwise with stirring under nitrogen at 0°C. The reaction was stirred for 3 hours at 0°C and a yellow precipitate was formed. The reaction was quenched with concentrated hydrochloric acid and then poured into ice water. The solid was filtered, washed with water and air dried to give 6-(2,4,6-trifluorophenyl)-8*H*-pyrido[2,3-c]pyridazine-5,7-dione as a yellow solid (1.9 2g), m.p. >330°C, still containing some THF, which was used without further purification.

^{1}H NMR (D_6-DMSO) δ ppm: 7.30 (m,2H), 8.10 (d,1H), 9.20 (d,1H), 11.90 (bs,1H), 12.60 (s,1H).

Step 4

The product from Step 3 (0.060 g) was heated to 90°C in phosphorus oxychloride (1 ml) for 1 hour to give a clear black solution. The mixture was cooled and the excess in phosphorus oxychloride evaporated. The residue was quenched with ice and aqueous sodium bicarbonate, extracted with ethyl acetate, the extract dried over magnesium sulphate and evaporated to give 5,7-dichloro-6-(2,4,6-trifluorophenyl)-pyrido[2,3-c]pyridazine as a black solid (0.087 g).

^{1}H NMR ($CDCl_3$) δ ppm: 6.90 (m,2H), 8.30 (d,1H), 9.75 (d,1H).

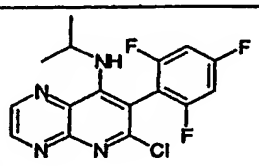
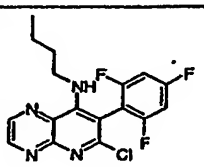
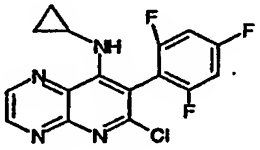
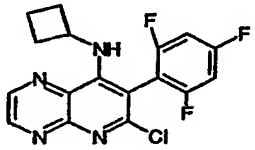
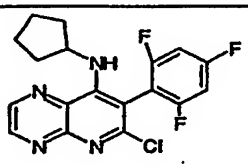
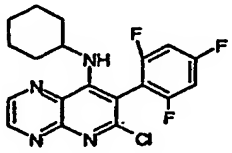
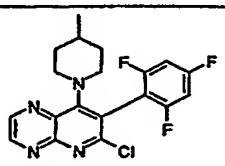
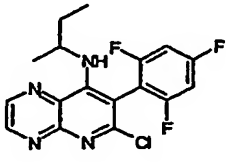
Step 4

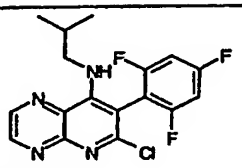
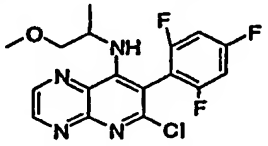
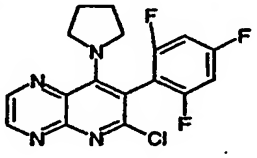
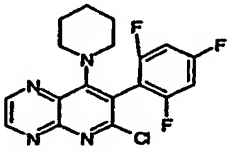
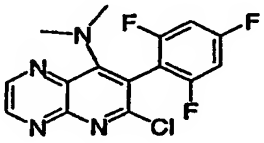
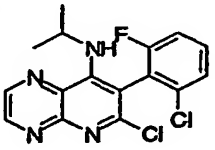
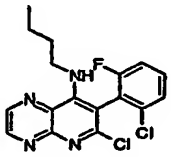
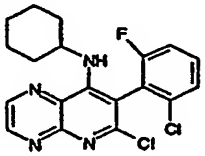
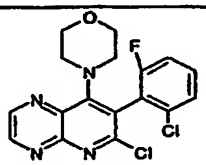
The product from Step 3 (0.080 g) was stirred with isopropylamine (2 ml) in DCM (5 ml) at room temperature overnight and then heated to 40°C in a sealed tube for 4 hours. The volatiles were evaporated, water was added and the mixture extracted with DCM. The extracts were dried over magnesium sulphate and evaporated to give a dark brown tar, which was purified by preparative TLC on silica gel plates eluting with ethyl acetate:hexane 3:2 to give

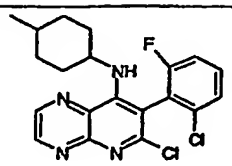
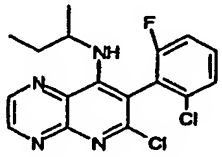
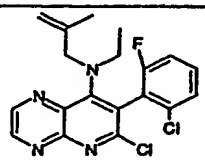
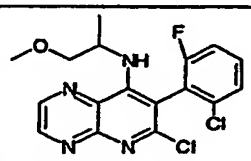
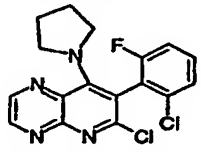
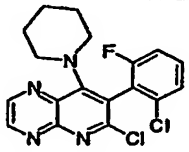
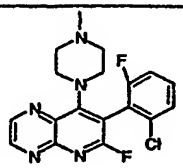
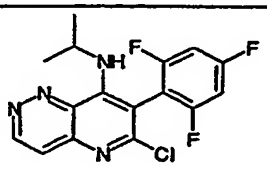
[7-Chloro-6-(2,4,6-trifluorophenyl)-pyrido[2,3-c]pyridazin-5-yl]-isopropylamine (0.008 g),

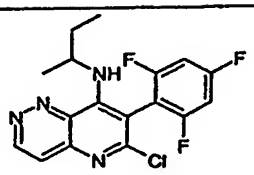
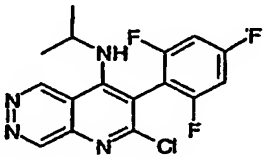
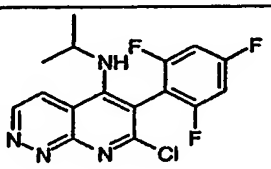
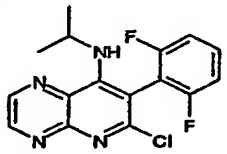
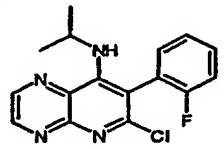
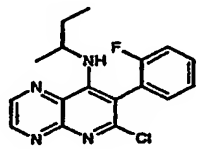
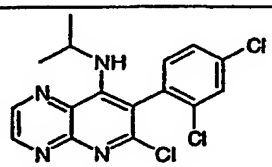
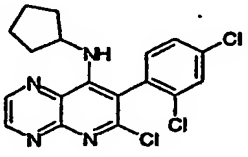
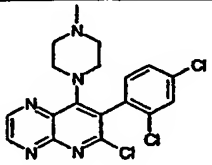
^{1}H NMR ($CDCl_3$) δ ppm: 1.20 (d,6H), 3.71 (m,1H), 4.45 (bs,1H), 6.87-6.92 (m,2H), 7.97 (d,1H), 9.37 (d,1H).

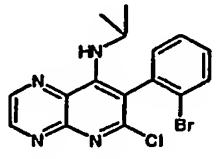
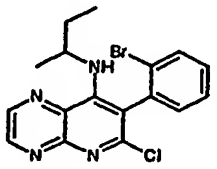
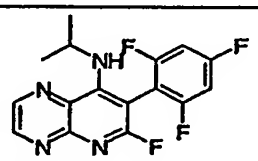
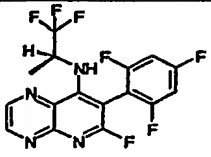
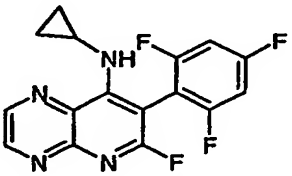
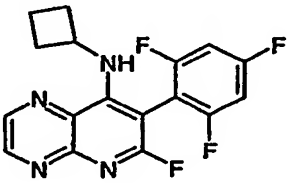
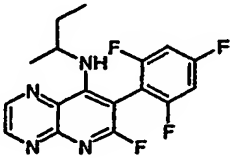
Table 133

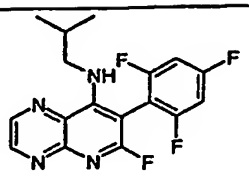
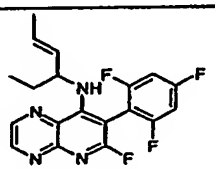
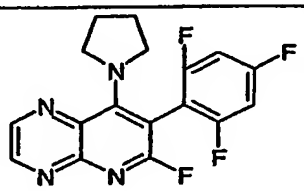
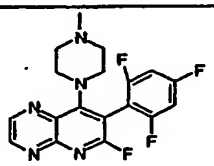
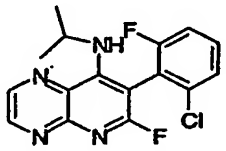
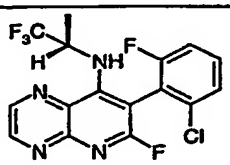
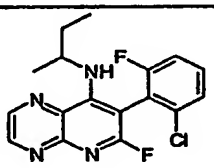
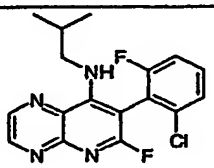
Compound No.	Table No.	Compound Structure	NMR data (ppm, in $CDCl_3$, unless otherwise stated) or Mpt.
3	1		1.1 (d,6H), 3.26 (m,1H), 6.84 (m,2H), 6.95 (bd,1H), 8.67 (d,1H), 9.0 (d,1H).
4	1		0.8 (t,3H), 1.27 (m,2H), 1.55 (m,2H), 2.87 (m,2H), 6.8,6.85 (ABd,2H); 8.66, 8.99 (ABd,2H).
14	1		129-131°C
15	1		149-150 °C
16	1		175-177 °C
17	1		153-155 °C
22	1		0.92 (m) + 1.22 (m) +1.55 (m) (total = 8H), 2.9 (m,2H), 6.85 (m,2H), 8.78,8.96 (ABd,2H).
23	1		151-153 °C

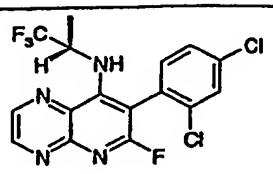
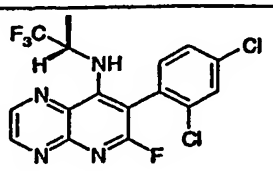
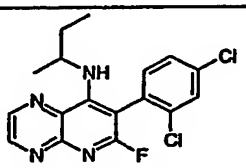
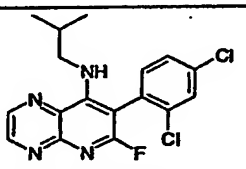
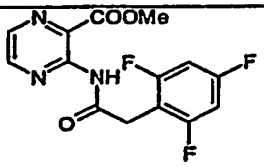
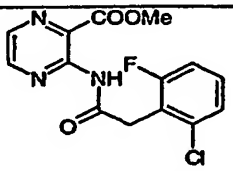
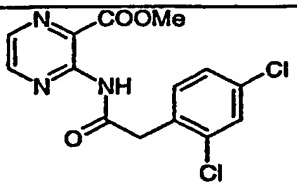
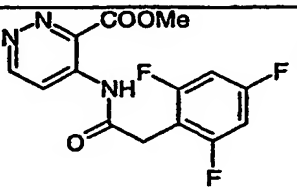
58	1		102-104 °C
108	1		1.12 (d,3H), 3.27 (m,2H), 3.3 (s,3H), 3.5 (m,1H), 6.8 (m,2H), 8.67 (d) + 8.97 (ABd) (total = 2H)
161	1		138-140 °C
162	1		140-141 °C
219	1		3.0 (s,6H), 6.85 (m,2H), 8.65,8.87 (ABd,2H)
3	5		157-159 °C
4	5		0.82 (m,3H),1.22 m + 1.5 m (total = 4H), 2.82 (m,2H), 7.1-7.47 (m,3H), 8.67 + 9.05 (ABd ,2H).
17	5		159-160 °C
20	5		166-168 °C

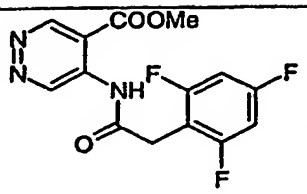
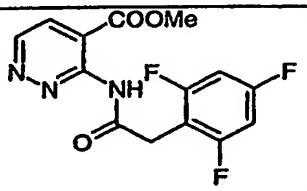
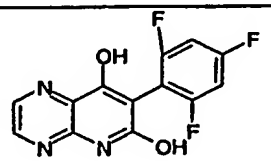
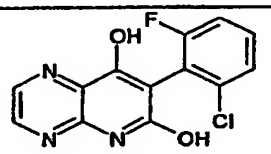
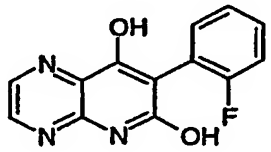
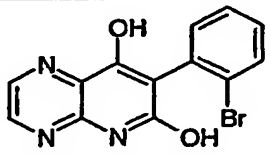
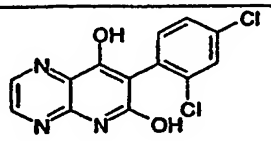
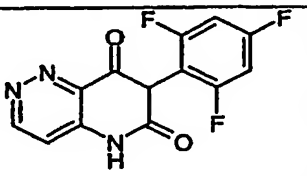
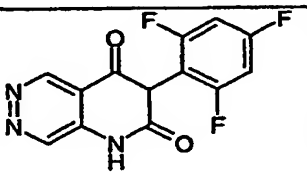
22	5		163-165 °C
23	5		163-165 °C
28	5		71-73 °C
108	5		1.05 (d) + 1.12 (d) (total = 3H), 3.1-3.5 (m,3H), 3.25 (d) + 3.32 (d) (total = 3H), 7.1 (m) + 7.4 (m) (total = 4H), 8.67 (d,1H), 9.06 (d,1H)
161	5		0.82 (m,4H), 3.65 (m,4H), 7.12-7.35 (m,3H), 8.66 + 8.87 (ABd,2H).
162	5		1.52 (m,6H), 3.3 (m,4H), 7.25 (m) + 7.4 (m) (total = 3H), 8.78 + 8.95 (ABd,2H).
171	5		2.3 (s,3H), 2.5 (m,4H), 7.15 (m,1H), 7.37 (m,2H), 8.75 (d,1H), 8.92 (d,1H).
3	11		1.16 (d,6H), 3.41 (m,1H), 6.85 (dd,2H), 7.79 (bs,1H), 7.84 (d,1H). 9.40 (d,1H).

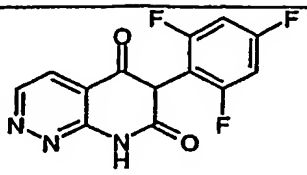
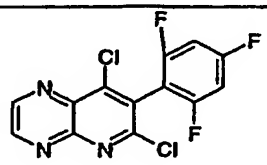
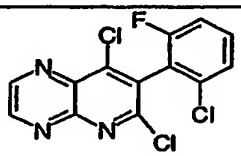
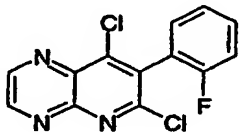
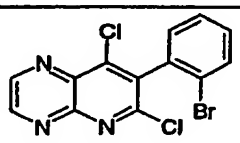
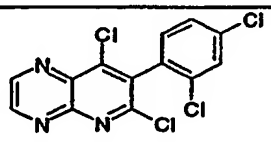
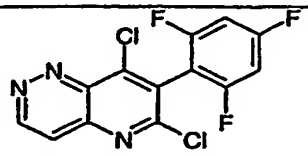
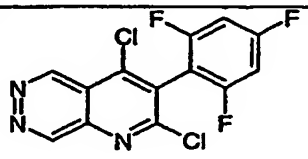
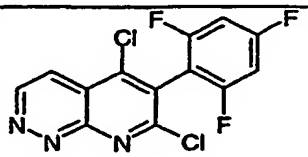
23	11		0.79 (t,3H), 1.11 (d,3H), 1.47 (m,2H), 3.13 (m,1H), 6.86 (dd,2H), 7.79 (bs,1H), 7.84 (d,1H), 9.40 (d,1H).
3	21		1.27 (d,6H), 4.05 (m,1H), 4.90 (bs,1H), 6.92 (m,2H), 9.55 (s,1H), 9.90 (s,1H).
3	26		1.20 (d,6H), 3.71 (m,1H), 4.45 (bs,1H), 6.87-6.92 (m,2H), 7.97 (d,1H), 9.37 (d,1H).
3	31		1.25 (d,6H), 4.5 (bd,1H) 4.6 (m,1H), 7.15 (t,2H), 7.6 (m,1H), 8.625 (fd,1H), 8.85 (fd,1H).
3	32		1.10 (d,6H), 4.52 (m,2H), 7.28 (m,3H), 7.47 (m,1H), 8.52 (d,1H), 8.76 (d,1H)
23	32		0.78 (m,3H), 1.07 (m,3H), 1.45 (m,2H), 4.48 (m,2H), 7.25 (m,3H), 7.50 (m,1H), 8.51 (d,1H), 8.71 (d,1H)
3	37		160-161 °C
16	37		181-183 °C
171	37		2.3 (s,3H), 2.5 (m,3H), 3.2-3.5 (m,4H), 7.27 (m) + 7.4 (m) + 7.62 (m) (total = 3H), 8.77 (d,1H), 8.92 (d,1H).

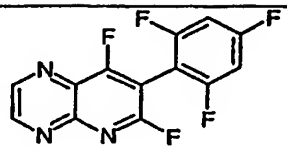
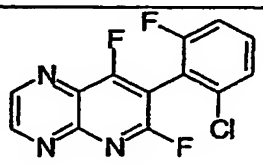
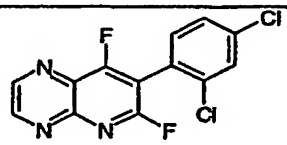
3	43		1.10 (d,6H), 4.32 (d,1H), 4.57 (m,1H), 7.22 (m,1H), 7.35 (m,1H), 7.48 (m,1H), 7.78 (m,H), 8.53 (d,1H), 8.71 (d,1H)
23	43		0.81 (m,3H), 1.10 (m,3H), 1.40 (m,2H), 4.26 (m,1H), 4.45 (m,1H), 7.25 (m,1H), 7.38 (m,1H), 7.50 (m,1H), 7.76 (m,1H), 8.52 (d,1H), 8.74 (d,1H)
3	103		127-128°C
5	103		138-140°C
12	103		106-108 °C
14	103		120-121°C
15	103		153-154°C
23	103		101-102 °C

58	103		99-100 °C
92	103		1.07 (t,3H), 1.57 (s,3H), 3.52 (s,2H), 3.72 (q,2H), 4.85 (m,2H), 6.85 (m,2H), 8.8 (d,1H), 9.0 (d,1H).
161	103		148-150°C
171	103		167-160 °C
2651	103		100-101 °C
2660	103		1.3 (d,3H), 1.4 (d,3H), 3.9 (m,1H), 6.95-7.6 (m,4H), 8.75 (m,1H), 9.05 (m,1H).
2671	103		123-124°C
2706	103		0.8 (m,6H), 1.72 (m,1H), 2.6 (m,2H), 7.02 - 7.47 (m,4H), 8.6 (d,1H), 8.92 (d,1H).

43704	103		133-135 °C (diastereoisomer 1)
43704	103		137-139 °C (diastereoisomer 2)
43715	103		118-119 °C
43750	103		0.80 (d) + 0.83 (d) (total = 6H), 1.72 (m,1H), 2.65 (m,2H), 7.1-7.3 (m) + 7.35,7.6 (d) (total = 3H), 8.6 (d,1H), 8.92 (d,1H).
1	128		4.03 (s,5H), 6.74 (t,2H), 8.43 (d,1H), 8.61 (d,1H) 10.9 (s,1H).
6	128		162-163°C
12	128		158-159°C
13	128		1.48 (t,3H), 4.52 (q,2H), 6.73 (d,1H), 8.75 (d,1H).

25	128		1.45 (t,3H), 3.90 (s,2H), (4.45 (q,2H), 6.75 (m,2H), 9.45 (s1H), 10.60 (s,1H), 11.1 (bs,1H).
37	128		1.40 (t,3H), 4.22 (s,2H), 4.41 (q,2H), 6.70 (m,2H), 7.94 (d,1H), 9.15 (d,1H), 10.30 (bs,1H).
1	129		(d^6-DMSO) 7.25(t,2H), 8.6(fd,1H),8.7(fd,1H), 12.6(s,1H).
6	129		>220°C
9	129		250-252 °C
11	129		258 °C
12	129		>200 °C
13	129		(CD_3OD) 6.83 (2d,2H), 7.44 (d,1H), 9.00 (d,1H).
25	129		(d^6-DMSO) 7.25 (m,2H), 9.17 (s,1H), 9.47 (s,1H), 12.30 (bs,1H).

37	129		(D_6-DMSO) 7.30 (m,2H), 8.10 (d,1H), 9.20 (d,1H), 11.90 (bs,1H), 12.60 (s,1H).
1	130		139-141°C
6	130		154-155°C
9	130		7.21(m,1H), 7.28(m,2H), 7.48(m,1H), 8.95(d,1H), 9.08(d,1H).
11	130		7.18(d, 1H), 7.29(m,1H), 7.41(t,1H), 7.69(dd,1H), 9.00(d,1H), 9.09(d,1H).
12	130		159-160°C
13	130		6.92 (m,2H), 8.11 (d,1H), 9.71 (d,1H).
25	130		6.90 (m,2H), 9.80 (s,1H), 10.0 (s, H).
37	130		6.90 (m,2H), 8.30 (d,1H), 9.75 (d,1H).

1	131		120-121°C
6	131		7.27 (m) + 7.55 (m) (total = 3H), 9.07 (d,1H), 9.2 (d,1H).
12	131		7.45 (m) + 7.67 (d) (total = 3H), 9.07 (d,1H), 9.2 (d,1H).

EXAMPLE 6

This Example illustrates the fungicidal properties of the compounds of the general formula (1).

Compounds were tested in a leaf disk assay, with methods described below. Test compounds were dissolved in DMSO, and diluted into water to 200 ppm.

Plasmopara viticola (downy mildew of grapevine): grapevine leaf disks were placed on agar in a 24-well plate and sprayed a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed seven days after inoculation as preventive fungicidal activity.

Phytophthora infestans (late blight of potato on tomato): tomato leaf disks were placed on water agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Erysiphe graminis f.sp. hordei (barley powdery mildew): barley leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Erysiphe graminis f.sp. tritici (wheat powdery mildew): wheat leaf segments were placed

on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Puccinia recondita f.sp. tritici (wheat brown rust): wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed nine days after inoculation as preventive fungicidal activity.

Septoria nodorum (wheat glume blotch): wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Pyrenophora teres (barley net blotch): barley leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Pyricularia oryzae (rice blast): rice leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

Botrytis cinerea (grey mould): bean leaf disks were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

The following compounds gave greater than 60% control of disease:

Plasmopara viticola, Compounds 4 (1), 20 (1), 23 (5);

Phytophthora infestans, Compounds 3 (1), 58 (5), 3 (103);

Erysiphe graminis f.sp. hordei, Compounds 3 (1), 14 (1), 15 (1), 16 (1), 17 (1), 22 (1), 23 (1), 58 (1), 108 (1), 161 (1), 162 (1), 3 (5), 4 (5), 17 (5), 20 (5), 22 (5), 23 (5), 28 (5), 58 (5), 108 (5), 162 (5), 171 (5), 665 (31), 23 (32), 3 (37), 16 (37), 171 (37), 665 (37), 678 (37), 3 (43), 23 (43), 685 (43), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103;

Erysiphe graminis f.sp.tritici, Compounds 3 (1), 4 (1), 15 (1), 16 (1), 22 91), 23 (1), 58 (1), 108 (1), 162 (1), 219 (1), 58 95), 161 (5), 3 (31), 16 (37), 665 (37), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103);

Puccinia recondita f.sp. tritici, Compounds 3 (1), 14 (1), 15 (1), 16 (1), 17 (1), 23 (1), 58 (1), 108 (1), 161 (1), 162 (1), 4 (5), 17 (5), 23 (5), 28 (5), 58 (5), 108 (5), 3 (31), 16 (37), 665 (37), 678 (37), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23855 (103), 23890 (103);

Septoria nodorum, Compounds 3 91), 15 (1), 16 (1), 17 (1), 23 (1), 58 (1), 58 95), 161 (5), 22 (6), 665 (37), 685 (43), 12 (103), 23 (103), 58 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23855 (103), 23890 (103);

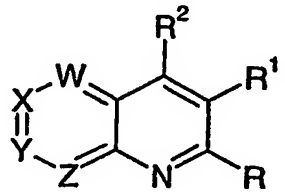
Pyrenophora teres, Compounds 3 (1), 14 (1), 15 (1), 16 (1), 17 (1), 23 (1), 58 (1), 161 (1), 3 (5), 20 (5), 16 (37), 665 (37), 3 (103), 12 (103), 23 (103), 58 (103), 2651 (103), 2660 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23855 (103), 23890 (103);

Pyricularia oryzae, Compounds 3 (1), 4 (1), 14 (1), 15 (1), 16 (1), 17 (1), 20 (1), 23 (1), 58 (1), 108 (1), 161 (1), 3 (5), 4 (5), 20 (5), 23 (5), 58 (5), 108 (5), 3 (32), 3 (37), 16 (37), 678 (37), 3 (43), 3 (103), 12 (103), 23 (103), 58 (103), 92 (103), 171 (103), 2651 (103), 2669 (103), 2671 (103), 23844 (103) diastereoisomer 1, 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103);

Botrytis cinerea, Compounds 4 (1), 14 (1), 15 (1), 16 (1), 17 (1), 22 (1), 58 (1), 108 (1), 4 (5), 22 (5), 28 (5), 58 (5), 108 (5), 162 (5), 16 (37), 678 (37), 23 (103), 92 (103), 2651 (103), 2660 (103), 23844 (103) diastereoisomer 2, 23855 (103), 23890 (103).

CLAIMS

1. The compound of the general formula (1):



(1)

wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is halo, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C_{1-4})alkyl, aryl(C_{1-4})alkoxy, heteroaryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkoxy, aryl(C_{1-4})alkylthio, heteroaryl(C_{1-4})alkylthio, morpholino, piperidino or pyrrolidino;

R^2 is NR^3R^4;

R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6, provided that not both R^3 and R^4 are H or NR^5R^6, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine *S*-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and

any of the foregoing aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'''R'''', -NHCOR''', -NHCONR'''R'''', -CONR'''R'''', -SO_2R''', -OSO_2R''', -COR''', -CR'''=NR'''' or -N=CR'''R'''', in which R''' and R'''' are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.

2. A compound according to claim 1 wherein W and Z are N and X and Y are CH.

3. A compound according to any one of the preceding claims wherein
R^3 is C_{1-8} alkyl, halo(C_{1-8})alkyl, hydroxy(C_{1-8})alkyl, C_{1-4} alkoxy(C_{1-8})alkyl, C_{1-4} alkoxyhalo-(C_{1-8})alkyl, tri(C_{1-4})alkylsilyl(C_{1-6})alkyl, C_{1-4} alkylcarbonyl(C_{1-8})alkyl, C_{1-4} alkylcarbonyl-halo(C_{1-8})alkyl, phenyl($_{1-4}$)alkyl, C_{2-8} alkenyl, halo(C_{2-8})alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl optionally substituted with chloro, fluoro or methyl, C_{3-8} cycloalkyl(C_{1-4})alkyl, phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and
R^4 is H, C_{1-4} alkyl, halo(C_{1-4})alkyl or amino, or
R^3 and R^4 together form a C_{3-7} alkylene or alkenylene chain optionally substituted with methyl, or,
together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

4. A compound according to any one of the preceding claims wherein
R^1 is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, pyridyl optionally substituted with from one to four halogen atoms or with

from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, or piperidino or morpholino both optionally substituted with one or two methyl groups.

5. A compound according to claim 4 wherein R^1 is 2,6-difluorophenyl, 2-fluoro-6-chlorophenyl, 2,5,6-trifluorophenyl, 2,4,6-trifluorophenyl, 2,6-difluoro-4-methoxyphenyl or pentafluorophenyl.

6. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is halo, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C_{1-4})alkyl, aryl(C_{1-4})alkoxy, heteroaryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkoxy, aryl(C_{1-4})-alkylthio, heteroaryl(C_{1-4})alkylthio, morpholino, piperidino or pyrrolidino;

R^2 is NR^3R^4;

R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6, provided that not both R^3 and R^4 are H or NR^5R^6, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and
any of the aryl, heteroaryl, aryloxy or heteroaryl groups being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'"R"", -NHCOR'", -NHCONR'"R"", -CONR'"R"", -SO_2R'", -OSO_2R'", -COR'", -CR'"=NR"" or -N=CR'"R"", in which R'" and R"" are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.

7. A compound according to claim 1 wherein
W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;
R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;
R is halo;
R^1 is halo, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, C_{1-8} alkoxy, C_{1-8} alkylthio, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, heteroarylthio, aryl(C_{1-4})alkyl, aryl(C_{1-4})alkoxy, heteroaryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkoxy, aryl(C_{1-4})alkylthio, heteroaryl(C_{1-4})alkylthio, morpholino, piperidino or pyrrolidino;
R^2 is NR^3R^4;
R^3 is C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and
R^4 is H, C_{1-4} alkyl or amino, or
R^3 and R^4 together form a C_{4-6} alkylene chain optionally substituted with C_{1-4} alkyl or C_{1-4} alkoxy, or,
together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring;
any of the alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl,

C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and

any of the aryl or heteroaryl groups or moieties being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'''R'''', -NHCOR''', -NHCONR'''R'''', -CONR'''R'''', -SO_2R''', -OSO_2R''', -COR''', -CR'''=NR'''' or -N=CR'''R'''', in which R''' and R'''' are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.

8. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is optionally substituted phenyl;

R^2 is NR^3R^4;

R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6, provided that not both R^3 and R^4 are H or NR^5R^6, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6}

alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C_{1-4} alkyl (especially methyl), and

any of the aryl or heteroaryl groups or moieties, including the phenyl group of R^1, being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, hydroxy(C_{1-6})alkyl, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR'''R'''', -NHCOR''', -NHCONR'''R'''', -CONR'''R'''', -SO_2R''', -OSO_2R''', -COR''', -CR'''=NR'''' or -N=CR'''R'''', in which R''' and R'''' are independently hydrogen, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, C_{1-4} alkylthio, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C_{1-4} alkyl or C_{1-4} alkoxy.

9. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

R^1 is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, pyridyl optionally substituted with from one to four halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, 2- or 3-thienyl optionally substituted with from one to three halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy, or piperidino or morpholino both optionally substituted with one or two methyl groups;

R^2 is NR^3R^4;

R^3 is C_{1-8} alkyl, halo(C_{1-8})alkyl, hydroxy(C_{1-8})alkyl, C_{1-4} alkoxy(C_{1-8})alkyl, C_{1-4} alkoxyhalo-(C_{1-8})alkyl, tri(C_{1-4})alkylsilyl(C_{1-6})alkyl, C_{1-4} alkylcarbonyl(C_{1-8})alkyl, C_{1-4} alkylcarbonyl-halo(C_{1-8})alkyl, phenyl($_{1-4}$)alkyl, C_{2-8} alkenyl, halo(C_{2-8})alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl optionally substituted with chloro, fluoro or methyl, C_{3-8} cycloalkyl(C_{1-4})alkyl, phenylamino,

piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and

R^4 is H, C_{1-4} alkyl, halo(C_{1-4})alkyl or amino, or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with methyl, or,

together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

10. A compound according to claim 1 wherein

W and X, W and Z, X and Y or Y and Z are N and the other two are CR^8;

R^8 is H, halo, C_{1-4} alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkyl;

R is halo;

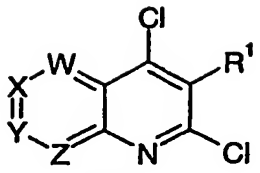
R^1 is phenyl optionally substituted with from one to five halogen atoms or with from one to three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy or halo(C_{1-4})alkoxy;

R^2 is NR^3R^4;

R^3 is C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl or phenylamino in which the phenyl ring is optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and

R^4 is H, C_{1-4} alkyl or amino, or R^3 and R^4 together form a C_{4-6} alkylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine ring.

11. A process for preparing a compound of the general formula (1) according to claim 1 wherein R is chloro or fluoro and R^2 is NR^3R^4 and W, X, Y, Z, R^1, R^3 and R^4 are as defined in claim 1, which comprises reacting an amine of the general formula NR^3R^4 with a compound of the general formula (6) or (13)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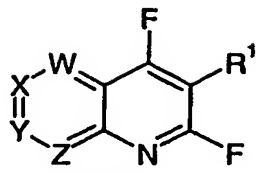
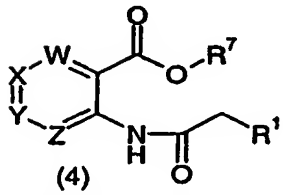

(13)

12. The intermediate chemicals having the general formulae (4), (5), (6) and (13):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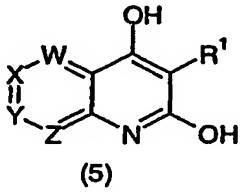
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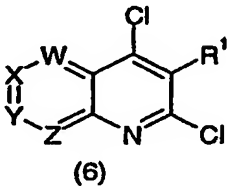
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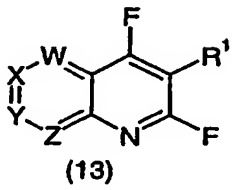
(13)

wherein W, X, Y, Z and R^1 are as defined in claim 1 and R^7 is C_{1-4} alkyl, other than the compound of formula (6) wherein X and Y are N, W and Z are C-Cl and R^1 is Cl.

13. A plant fungicidal composition comprising a fungicidally effective amount of a compound as defined in claim 1 and a suitable carrier or diluent therefor.

14. A method of combating or controlling phytopathogenic fungi which comprises applying to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or to any other plant growth medium, a fungicidally effective amount of a compound according to claim 1 or a composition according to claim 13.